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EXPERIMENTAL PRODUCTION AND SPECIFIC TREATMENT OF GALL-BLADDER DISEASE

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EXPERIMENTAL studies on gall-bladder disease have evolved along three lines of approach: stasis, metabolic disturbances, and infection. Some observers maintain that stasis is a provocative cause and that metabolic disturbances underlie the problem of cholelithiasis. However, to explain infectious gall-bladder disease and the two previous approaches demands the presence of an exciting factor. Today, many clinicians are prone to consider various forms of bacteria to be that exciting factor. The literature is full of references on the subject (3). Judd, Rosenow, Blalock, Branch, Brown, Burden, Drennan, Friesleben, Taylor and Whitby, Illingworth, Magner and Hutcheson, Moynihan, Williams and McLachlan, Wilkie, Huntemuller (2), Gundermann (1), and many others have emphasized this association.

It is apparent from the literature that various workers obtained divergent percentage results in their bacterial studies on gall bladders removed at operation. In a former communication (3) we have considered this in detail. It is striking to note how the sum total falls into certain groups of organisms. These are the streptococcus, staphylococcus, colon-typhoid, and certain anaerobic groups. When more carefully considered these groups might well be further divided according to those causing acute infectious diseases, to those found in the foci of the head, and to those found in the lower intestines.

In the earlier studies on this subject an attempt was made to produce gall-bladder disease by the intravenous injection of relatively massive amounts of live bacteria in laboratory animals. Too often such methods defeated the purpose of the investigation and resulted in deaths or acute lesions, neither of which resembled the chronic disease found in man. Gradually we learned to give smaller amounts and in January, 1935, (3) reported observations on a series of bacteria derived from various sources and resembling those reported in the literature which were found in culturing the gall bladders removed by surgeons. It is apparent from Table I that chronic cholecystitis has been reproduced in laboratory animals following the introduction of strains of some types reported as possible causative agents. At present we have used 105 antigens and nearly 1,500 animals.

For the past 2½ years our methods have been revised. We have chosen the Flemish giant rabbit. They are placed in individual cages, numbers tattooed on the ear, their tem-

From the Frankford Foundation for Medical Research, Philadelphia.

perature, weight, physical condition noted twice a week, or more often if sick, their appetite noted daily and special individual examinations done and recorded every 2 weeks. In this way a case report similar to a case history is compiled. Gradually one becomes familiar with the differences between a sick and well rabbit, competent to judge joints and the like. The amount of bacteria injected has been decreased to 0.02 cubic centimeter and 0.05 cubic centimeter of an 18 to 24 hour broth culture. Such injections are given once or twice a week over a 3 to 6 months' period, or less, if the rabbit becomes ill. We watch the sick animals every 6 hours in order that postmortem examinations and notes may be made efficiently. Occasionally a very sick rabbit is killed to prevent postmortem changes when death seems imminent. We have chosen to use one organism, a non-hemolytic streptococcus obtained from a stool culture, because in our earlier work gall-bladder disease occurred in 20 per cent of the animals following its introduction. We have attempted to simulate the condition as it may exist in the human subject who has frequent minor infections by giving small repeated intravenous injections. We realize that it is almost impossible to duplicate focal infection as it exists in man.

In this study now to be reported, notice the marked difference following the change in our methods (Table II). The number of injections given varied from 1 to 51, the average being 16.3 per rabbit. The incidence of gall-bladder disease arose from approximately 20 to 50 per cent. The smaller percentage of recovered cultures would logically follow the production of a more chronic lesion.

It is striking to note the incidence of disease in other organs especially the kidneys and joints. We have seen practically every organ or system affected at one time or another—varying from paralysis with spasticity, vegetative endocarditis, gastric ulcer, lung abscess, to infected nodes. This seems all the more significant when one considers how seldom a case of clinical cholecystitis is unaccompanied by other lesions. The accompanying photomicrographs (Figures 1, 2, 3, 4, 5) illustrate the various forms of chronic cholecystitis as produced.

However, there was no constant histological picture. Usually the muscle coat became thicker, but any or all coats may be involved. Leucocytic infiltration of varying degrees may affect all or any coat. The epithelium may be normal, desquamated, or eroded. Pericholecystitis, empyema, perforation, and gall stones occurred occasionally.

The question then arose that perhaps some of these lesions might arise from bacterial emboli in the smaller arterioles and might not be the result of live bacteria *per se*. We selected two groups, each consisting of 10 healthy rabbits and gave massive intravenous injections every other day for a period of 3 months. One group received an autogenous vaccine, the other an autogenous filtrate made from the non-hemolytic streptococcus being investigated. An average of 5,200 million bacterial bodies were given to each rabbit in the first group. At autopsy one rabbit had a sterile caseous mass in the lower right lung and moderate pitting of the kidney surface. The other abnormal animal had marked pitting of the kidney surface. Its cut surface was

TABLE I.—VARIOUS BACTERIA USED IN ATTEMPT TO PRODUCE EXPERIMENTAL GALL-BLADDER DISEASE

Organism	Strains used	Rabbits used	Diseased gall bladders	Positive bile cultures
Bacillus coli	8	11	4	6
Bacillus pyocyaneus	1	2	1	2
Bacillus mucosus capsulatus	1	1	0	0
Streptococcus hæmolyticus	12	17	2	2 (1 ?)
Streptococcus non-hæmolyticus	5	70	14	9 (1 ?)
Streptococcus viridans	13	17	2	0 (1 ?)
Staphylococcus aureus	4	11	2	3 (2 ?)
Totals	44	129	25	22

?With some slightly different characteristic from original.

TABLE II.—AUTOPSY FINDINGS STREPTOCOCCUS NON-HEMOLYTICUS INJECTIONS

	Number	Per cent
Rabbits used	166	
Diseased gall bladders	84	50.6
Organisms recovered from bile	25	15.0
Diseased kidneys	58	
Diseased joints	110	

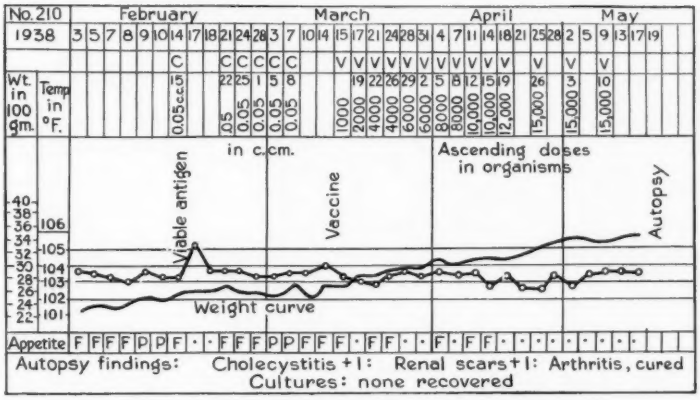


Chart 1. Method of keeping rabbit's record.

streaked with white lines, the cortex definitely narrowed. In the other group each animal received 4.1 cubic centimeters of 1:50 dilution of filtrate. The only abnormal finding was moderate pitting of the kidney surface in one instance. In none was an abnormal gall bladder found. Cultures from bile and kidneys were negative. Therefore, we felt that such diseased processes described must be ascribed in a large measure to the live bacteria.

In a former report (4) on immunological studies with this organism we showed that joint lesions and to a less extent gall-bladder disease were lessened in those animals which received a small series of vaccine and filtrate injections prior to inoculation. We wondered whether treatment of sick animals with such preparations would be of value. The attempt to determine whether gall-bladder disease was present prior to treatment was made by separate roentgenographic study (R. M. Smith and G. M. Nelson). There was found to be a 33 per cent error in such diagnoses and, since the incidence of its production had exceeded 50 per cent, we segregated the sick animals into groups of threes: control, vaccine, and filtrate. Such a selection depended upon clinical observations, the number of bacterial injections, the temperature variations, weight loss, and joint disease. An attempt was made to give preferences to the control group and to select three treated alike and those sick alike from the clinical viewpoint (Table III).

The care of all groups as regards feeding and observations was identical. The vaccine group received at planned intervals and for an elective duration intradermal doses of the autogenous vaccine. Likewise the filtrate group received 1:50 and 1:100 dilutions of the autogenous filtrate. Autopsy examinations of all animals were made at the same date unless death or extreme illness prevented. In Table III we have compiled the findings of the three groups so treated according to self-evident gross pathological findings from the autopsy records. To avoid error we have included only the kidney, joint, gall-bladder, and cultural findings since they are so easy to detect. Any questionable lesion is not included. That preference was given to the control group is suggested when one notes that 7 of the 59 were found to be grossly normal at necropsy. When one deducts the number of normals from the total number, it is surprising to see how closely the number of diseased animals par allel each other in the three groups.

The incidence of gall-bladder disease is practically the same in the control and filtrate groups and less in the vaccine group. This might be explained as a result of the treatment received. Certainly one sees gross evidence of disease in many with a return of function if the appearance of the gall-bladder bile be a criterion. The smaller incidence of positive cultures in the bile would suggest such a conclusion. However, the most striking indi-

TABLE III.—COMBINED TREATMENT GROUPS—AUTOPSY FINDINGS

	Control		Vaccine		Filtrate	
	No.	Per cent	No.	Per cent	No.	Per cent
Number of rabbits	59	....	50	..	57	..
Number normal	7	....	2	..	2	..
Gall-bladder disease present	31	52.5	19	38	32	56
Cultures from bile	11	35.5	4	21	9	28
Kidney disease present	22	....	17	..	20	..
Cultures from kidneys and urine	5	....	1	..	5	..
Joint disease present	35	....	36	..	39	..
Cultures from joints	5	....	2	..	7	..
Cultures from any organ	17	29	6	10	16	28

TABLE IV.—AUTOPSY FINDINGS IN ANIMALS TREATED FOR PLANNED PERIOD

	Control		Vaccine		Filtrate	
	No.	Per cent	No.	Per cent	No.	Per cent
Number of rabbits	43	..	44	..	41	..
Number diseased	37	..	42	..	39	..
Gall-bladder disease present	25	58	19	43	26	63
Cultures from bile	6	24	3	43	6	23
Kidney disease present	16	..	13	..	10	..
Cultures from kidney	1	..	0	..	1	..
Joint disease present	29	..	34	..	30	..
Cultures from joints	2	..	1	..	3	..
Cultures from any organ	9	20	4	9	8	19

cation of the possible effect of treatment is noted in the sum total of animals from which positive cultures of the original non-hemolytic streptococcus was recovered at autopsy. In the vaccine group only 10 per cent were recovered, whereas from the control group 29 per cent, and from the filtrate group 28 per cent.

To make the analysis more complete, the rabbits which died or were killed during the treatment period were studied further. The death incidence in the vaccine group (6 rabbits) was markedly decreased while in the two other groups it was approximately equal (16 controls, 17 filtrates). Not one of those treated with vaccine had gall-bladder disease and only one positive bile culture was obtained, this being in a case of septicemia. In the control group gall-bladder disease was present in 6 of the 16 deaths and in the filtrate group in 6 of the 17, with positive bile cultures in 5 of the control group and in 3 of the filtrate group. The incidence of total positive cultures from all organs in the vaccine group was 33 per cent (2 of 6), while in the other groups it was

TABLE V.—AVERAGE WEIGHT, IN GRAMS, AND TEMPERATURE READINGS, FAHRENHEIT, OF ANIMALS LIVING TO TERM

	Control		Vaccine		Filtrate	
	Weight	Temperature	Weight	Temperature	Weight	Temperature
At outset	2954	103.3	2098	103.4	2979	103.1
1 month	3075	103.4	3095	103.4	3238	103.2
2 months	3925	103.3	3312	103.5	3531	103.3
Autopsy	3461	103.3	3540	103.3	3649	103.2

TABLE VI.—ANIMALS WITH JOINT DISEASE GOING TO TERM

	Control		Vaccine		Filtrate	
	No.	Per cent	No.	Per cent	No.	Per cent
Clinical findings—						
Rabbits	31	..	36	..	28	..
Improved	20	65	27	75	23	82
Unimproved	11	..	9	..	5	..
Autopsy findings—						
Cured	8	26	9	25	7	25
Improved	19	61	25	69	18	64
Purulent	4	13	2	6	3	11

approximately 50 per cent (8 of 16 controls and 8 of 17 filtrates).

A further analysis of the deaths in this group of rabbits killed or dying during treatment was made to determine the time interval between treatment and death. Four of the control group lived less than 1 month, with positive bile cultures in 1; 3 lived for a period of 1 to 2 months, with no positive bile cultures; 3 lived 2 to 3 months, with 1 positive bile culture; 6 lived 3 to 6 months, with 3 positive bile cultures. Of the vaccine group, 2 lived less than 1 month, with no positive bile cultures; 2 lived 1 to 2 months, with 1 positive bile culture; 1 lived 2 to 3 months, with no positive bile culture; and 1 lived 3 to 6 months, with no positive bile culture. Of the filtrate group 7 lived less than a month, with 3 positive bile cultures; 2 lived 1 to 2 months, 4 lived 2 to 3 months; and 4 lived 3 to 6 months, with no positive bile culture. In other words, 9 of the controls and 8 of the filtrate group lived longer than 2 months, whereas there were only 2 deaths in the vaccine group. This would suggest that treatment might have decreased the death rate in this group.

But to be more critical, in Table IV we have excluded all deaths, and the same trend was present.

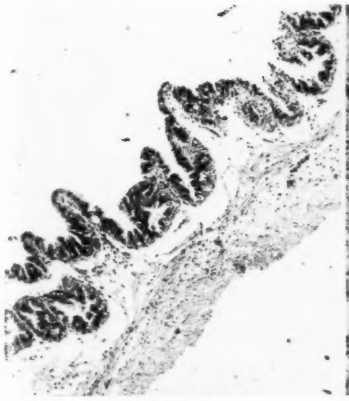


Fig. 1.

Fig. 2.

Fig. 3.

Fig. 1. Section from normal gall bladder of rabbit to illustrate various coats and thicknesses. ×60.

Fig. 2. Section taken from a markedly fibrous, and edematous gall-bladder wall showing atrophy of the mucosa and desquamation of the epithelium. ×60.

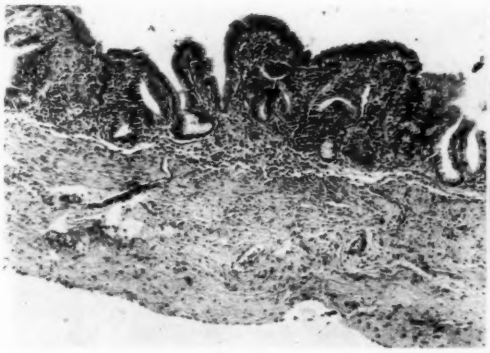
Fig. 3. A marked inflammatory reaction involving all coats. Note the extensive leucocytic infiltration of the mucosa. ×60.

The vaccine group had a lower percentage of gall-bladder lesions, a decrease in the relative positive bile and total cultures from all organs, whereas the other two groups still paralleled each other.

In Table V is to be found the total average weight and temperature readings of each group. The weight curve of the controls increased up to the second month and then decreased. The vaccine group and the filtrate group, but to a less degree, consistently increased. The temperature curves are similar.

In Table VI the composite findings of clinical and autopsy observations on joints are shown. There was very little difference when the autopsy findings were compared. These figures would be changed materially if one were to consider those dying during the course of treatment inasmuch as the mortality rate was greater in the control and filtrate groups.

We realized that the amount of vaccine and filtrate to administer was unknown. Soon we began to alternate groups under treatment giving 2,000 bacterial bodies and 0.05 cubic



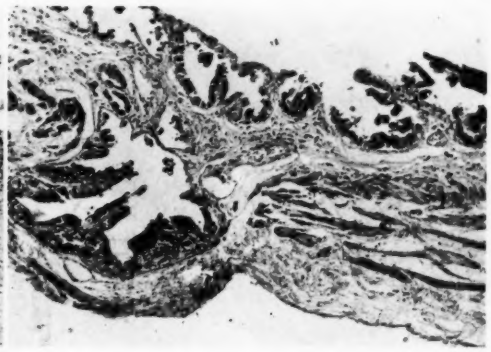


Fig. 4, left. A moderate thickening and fibrosis of the wall and a leucocytic infiltration of all coats. ×75.

Fig. 5. Slight thickening of the wall with edema. Note a slight mononuclear leucocytic infiltration of submucosa, atrophy of mucosa, and desquamation of the epithelium. ×75.

TABLE VII.—TREATMENT ANALYSIS—SMALL DOSES—AUTOPSY FINDINGS

	Control	Vaccine	Filtrate
Rabbits	22	23	27
Normal	1	0	1
Gall-bladder disease present	15	9	14
Positive bile cultures	1	1	4
Kidney disease present	9	10	11
Cultures from kidney	1	1	4
Joint disease present	17	17	17
Joint cultures positive	3	2	6
Total cultures from any organ	5	3	11
Died or killed	2	4	12
Gall-bladder disease present	0	0	4
Positive bile cultures	0	0	2

TABLE VIII.—TREATMENT ANALYSIS—LARGE DOSES—AUTOPSY FINDINGS

	Control	Vaccine	Filtrate
Rabbits	22	21	21
Normal	2	2	1
Gall-bladder disease present	11	9	13
Positive bile cultures	6	2	3
Kidney disease present	8	6	5
Positive cultures from kidney	2	0	1
Joint disease present	13	13	16
Positive cultures from joint	1	0	0
Total cultures from any organ	6	2	3
Killed or died	6	2	1
Gall-bladder disease present	3	0	1
Positive bile cultures	2	1	0

centimeter of 1:100 dilution of filtrate twice a week to one group and ascending doses twice a week to the other until 15,000 bacterial bodies and 0.3 cubic centimeter of the filtrate had been reached. In Table VII note that when small doses were given, the filtrate group had far more deaths, more positive bile and total cultures. The 2 other groups fairly well paralleled each other except that the incidence of gall-bladder disease was definitely less in the vaccine group.

In Table VIII note a smaller incidence of gall-bladder disease in the vaccine group, a smaller percentage of recoveries of organisms both from the bile and all organs, than in the other groups. The death rate remains low. The filtrate group has fewer organisms recovered and a definitely lower death rate than in the previous tables. It almost parallels the vaccine group and might suggest that the small doses were inadequate.

We deliberately varied the duration of treatment for the sake of comparison. In Table IX are those treated for 2 to 3 months. In comparing the vaccine with the control group the incidence of gall-bladder disease was materially less. The death rate and total number of organisms recovered from all organs was less. The filtrate group was relatively similar to the control except for definite increase in organisms recovered from all organs.

In Table X are those treated for 3 to 4 months. In comparing the vaccine and control groups, notice in those treated with vaccine a definite decrease in the incidence of all disease. In no instance was the non-hemolytic streptococcus recovered from the vaccine group. In comparing the filtrate with the control group there was very little difference.

Table XI includes those treated for a period of 4 to 6 months. The vaccine and filtrate groups paralleled in a general way the control group except for a definite decrease in the organisms obtained from the bile and all organs at autopsy. A comparison of these treatment periods would make one think the longer treatment intervals are the best.

During the course of treatment 72 rabbits were fed nothing but rolled oats for a period of 2½ months. This diet was inadequate in

TABLE IX.—TREATMENT ANALYSIS—2 TO 3 MONTHS—AUTOPSY FINDINGS

	Control	Vaccine	Filtrate
Rabbits	25	19	30
Normal	3	1	2
Gall-bladder disease present	16	7	16
Bile cultures positive	4	3	6
Kidney disease present	5	7	9
Positive cultures from kidney	3	1	5
Joint disease present	17	13	20
Positive cultures from joints	1	1	6
Total cultures from any organ	6	4	13
Died or killed	8	5	12
Gall-bladder disease present	3	1	4
Positive bile cultures	1	0	3

TABLE X.—TREATMENT ANALYSIS—3 TO 4 MONTHS—AUTOPSY FINDINGS

	Control	Vaccine	Filtrate
Rabbits	10	10	13
Normal	0	2	0
Gall-bladder disease present	7	4	10
Bile cultures positive	2	0	3
Kidney disease present	5	3	5
Kidney cultures positive	1	0	0
Joint disease present	9	4	9
Joint cultures positive	3	0	1
Total cultures from any organ	4	0	3
Died or killed	3	2	3
Gall-bladder disease present	2	0	1
Positive bile cultures	2	0	0

TABLE XI.—TREATMENT ANALYSIS—4 TO 6 MONTHS—AUTOPSY FINDINGS

	Control	Vaccine	Filtrate
Rabbits	24	21	14
Normal	3	0	1
Gall-bladder disease present	10	9	6
Bile cultures positive	5	1	0
Kidney disease present	10	7	6
Kidney cultures positive	1	0	0
Joint disease present	10	19	10
Joint cultures positive	1	1	0
Total cultures from any organ	7	2	0
Died or killed	1	0	2
Gall-bladder disease present	0	0	1
Positive bile cultures	0	0	0

certain vitamins. Following this period a preparation was fed containing vitamins A, B_1, D, E, and G. In Table XII you will note the uniform loss in weight in the 10 day period preceding its administration, as well as the uniform gain in all groups after the administration of this vitamin containing food.

In Table XIII is the record of the autopsy findings. The incidence of gall-bladder disease was considerably higher in all groups when compared to the combined groups (Table XI), whereas there was a lowering of the percentage of organisms recovered from the bile in all groups except the filtrate. It is also quite striking to note that only 3 rabbits in our entire vaccine group had gall-bladder disease at autopsy which did not fall into this group. There was no material increase in the incidence of kidney and joint disease in any group when compared to the total groups studied, and there was practically no difference in the percentage of positive organisms found in all organs as compared with the findings in the composite groups. One wonders whether a certain vitamin or vitamins, plus vaccine therapy might not be the responsible factors in the improvements noted in the vaccine group.

TABLE XII.—AVERAGE WEIGHT PER RABBIT BEFORE AND AFTER VITAMIN FEEDINGS

	Control	Vaccine	Filtrate
January 10	2677	2762	2820
January 20	2609	2687	2734
January 31	2942	2979	3041
Total loss in 10 days before	68	75	76
Total gain in 11 days after	333	292	207

TABLE XIII.—AVITAMINOSIS GROUP—AUTOPSY FINDINGS

	Control		Vaccine		Filtrate	
	No.	Per cent	No.	Per cent	No.	Per cent
Rabbits	24	..	25	..	23	..
Normal	2	..	2	..	2	..
Gall-bladder disease present	17	70	16	64	19	83
Bile cultures positive	3	18	2	13	6	32
Kidney disease present	11	..	9	..	7	..
Kidney cultures positive	1	..	1	..	4	..
Joint disease present	16	67	16	64	14	60
Joint cultures positive	1	..	..	..	1	..
Total cultures from any organ	5	20	2	8	7	30

SUMMARY

This study deals with one organism, a non-hemolytic streptococcus. We realize that a larger series is necessary before definite conclusions can be drawn, but it is hoped that in the interim, others will be sufficiently interested to parallel this tedious and time consuming investigation. From the data presented the following inferences may be temporarily deduced.

1. Chronic cholecystitis similar to the human forms has been produced. These lesions have been associated frequently with multiple lesions reminding us of the frequency in which one sees associated lesions in the clinical varieties of human cholecystitis.

2. Those animals treated with large doses of vaccine over a period of 3 months or more had a definitely smaller percentage of gross gall-bladder lesions and there was a definite decrease in the incidence of the recovery of the organism at autopsy.

3. Those animals treated with filtrate by and large were quite similar to the untreated group. There is some evidence to suggest that our dosage may have been too small.

4. Vitamins were necessary in all groups to maintain weight. In addition there is reason to believe that an adequate vitamin content in the diet combined with the administration of vaccine is necessary to control successfully this form of experimental cholecystitis.

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INTESTINAL POLYPS: PATHOGENESIS AND RELATION TO MALIGNANCY

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NUMEROUS classifications of polyps of the large intestine, based on the etiology, pathology, and clinical features have been attempted. Multiple polyps are frequently encountered in such an inflammatory disease as ulcerative colitis. The polyps of multiple adenomatosis of the large intestine have been thought to be different in origin and nature from those associated with this inflammatory disease. This is a comparative clinicopathological study of polyps occurring under these two conditions.

REVIEW OF LITERATURE

The earliest report of intestinal polyposis was made by Menzel in 1721, and during the following 150 years, Wagner, Rokitansky, Lebert, and Virchow described polyps of the intestine. Woodward, in 1881, emphasized that small polyps form during the phase of healing of chronic ulcerative colitis, whereas Cripps, in 1882, distinguished the condition which he called "disseminated polyposis" and noted an hereditary basis.

The results of earlier investigations suggested that intestinal polyps may be dissimilar both etiologically and pathologically, and undoubtedly accounted for the innumerable classifications that were later suggested. Those of Erdmann and Morris, and Susman are based on etiological and clinical considerations, whereas Schmieden and Westhues, Wesson and Bargen, and Lockhart-Mummery have proposed that polyps be classified on the basis of their pathological characteristics. Three basic concepts concerning the etiology of multiple adenoma of the large bowel exist: first, the hypothesis of Virchow that a hyperplastic response to inflammation produces the polyps; second, the opinion of Ribbert that the tumors originate from misplaced embryonal rests in the wall of the bowel; and finally, that chronic irritation in the presence of a congenital predisposition is necessary, as suggested by Verse. Genkin and Dmitruk, Hoelzel and Da Costa, have been successful in producing polyps experimentally in animals.

A heredofamilial disposition to multiple adenomatosis of the intestine has been noted repeatedly and Lockhart-Mummery believes that the condition is transmitted as a mendelian dominant characteristic. Hullsiek found evidence of a hereditary disposition in 11 per cent of 127 cases, whereas Mayo and Wakefield, in a review of 19 cases, found that 5 of the 38 parents had carcinoma of the colon. The congenital occurrence of the disease has never been substantiated by the demonstration of polyps at birth, although McKenney reported a case of a patient aged 2 years, and Kennedy and Weber found polyps in a child aged 2½ years.

Lockhart-Mummery and Dukes have stated that malignant changes always occur in cases of true multiple adenomatosis, whereas Soper found the incidence of carcinoma to be 43 per cent in such cases. McKenney found malignant changes in a third of his cases, whereas Felsen failed to observe this complication as frequently.

There has been general agreement concerning the pathology of multiple polyposis and the term, "multiple adenomatosis," as suggested by Lockhart-Mummery, seems more suitable inasmuch as it describes the pathological nature of the polyps. However, there is much disagreement concerning the pathogenesis of these tumors. The occurrence of tiny mammillations throughout the intestinal mucosa and also diffuse mucosal hyperplasia have been observed frequently. The association of enlarged lymph follicles and lymphocytic infiltration with the earliest manifesta-

Abridgment of thesis submitted by Dr. Coffey to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of M.S. in Medicine. Work done on the Intestinal Service, St. Mary's Hospital.

From The Mayo Foundation and the Division of Medicine, The Mayo Clinic.

Fig. 1. Localized region showing lengthening of the glands and benign hyperplasia. ×45.

tions of the polyps has been observed by Schmieden and Westhues, Fansler, Saint, and Feyrter.

The occurrence of polyps as the result of gross inflammation of the large intestine has been accepted generally as an entity distinct from multiple polyposis or adenomatosis. Bargen and Comfort found that polyps developed in 10 per cent of their cases of chronic ulcerative colitis and they emphasized that the polyps occur with the greatest frequency at the site of the most severe inflammation. Saint, on the other hand, was of the opinion that polyps were more prone to develop in the region of a mild, less destructive inflammatory process. Dukes, and Hewitt and Howard claimed that the polyps develop at the points at which the blood vessels pierce the wall of the bowel, an observation that Rankin failed to substantiate.

Bargen and Comfort demonstrated that the polyps in cases of chronic ulcerative colitis represent isolated regions of mucous membrane or granulation tissue which result from widespread sloughing of the mucous membrane of the colon. The pathological nature of these tumors has been studied by Brust and Bargen, who found that they were usually composed of granulation tissue and, in some instances, of mucosal remnants in which inflammatory hyperplasia was conspicuous. They added that true adenomas are relatively rare. Horgan, Wheeler, Buie, and Hurst have noted the development of true adenoma in

Fig. 2. Adenomatous change in several isolated glands; cellular infiltration is conspicuous. ×115.

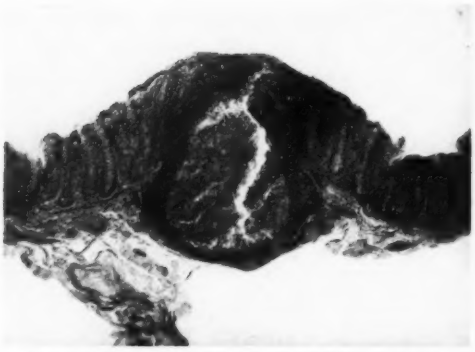
cases of chronic ulcerative colitis, whereas Felsen failed to identify adenoma in cases of bacillary dysentery in which polyps developed.

The importance of carcinoma as a complication of chronic ulcerative colitis has been stressed by one of us and malignant change has been noted in 2.5 per cent of a large series of cases. The hypothesis that a transition of inflammatory polyps to adenomatous polyps occurs, and that subsequently carcinoma develops has been offered. In a series of cases of chronic ulcerative colitis in which carcinoma developed, polyps were found in 60 per cent. Ewing, and Schmieden and Westhues have failed to observe any instance of malignant change in cases of chronic ulcerative colitis.

METHODS

A comparative clinicopathological study of the two types of polyps was carried out:

Multiple adenomatosis. Those cases of multiple polyposis of the colon, in which a history of antecedent inflammation of the colon was lacking and which were encountered at the



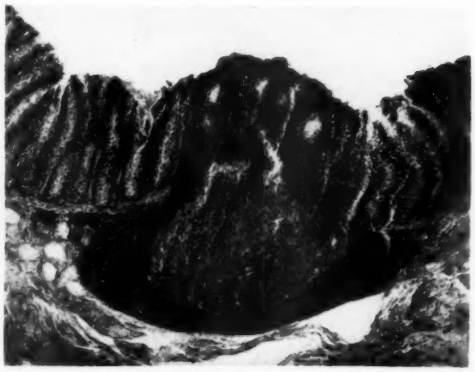


Fig. 3. a, left. Hyperplastic lymph follicle which has ruptured through the muscularis mucosa and has caused protrusion of the overlying mucosa. ×37. b, Hyperplastic lymph follicle associated with adenomatous change in several of the glands which were in the overlying mucosa. ×40.

clinic during the years 1930 to 1934 inclusive, were selected. A survey of salient clinical features was made and the available pathological specimens were studied in regard to their pathogenesis and their pathological nature.

Chronic ulcerative colitis with polyposis. Cases were chosen from two periods, namely 1913 to 1923, inclusive, and 1932 to 1934, inclusive, in order to determine the influence, if any, of more recent modes of treatment of chronic ulcerative colitis on the incidence of polyposis. Significant clinical features of these cases were reviewed and the available pathological material was studied grossly and microscopically.

RESULTS

Multiple adenomatosis. Of the 29 patients, 69 per cent were males. Fifty-two per cent were in the first 2 decades of life and 17 per cent were in the third decade. The youngest was 9 years and the oldest 71 years old.

Fig. 4. Chronic ulcerative colitis; polypoid tufts of mucosa with complete destruction of the mucosa in the adjacent region.

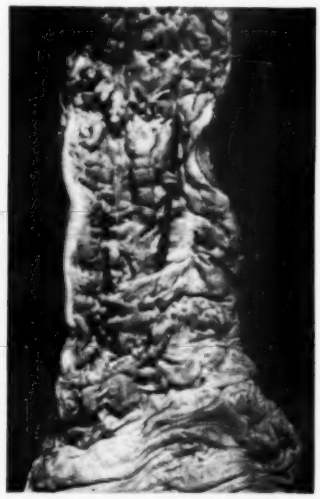


Fig. 5. Chronic ulcerative colitis; polyps in which their bridge-like structure is demonstrated. Bridges of mucosa and granulation tissue are often formed.

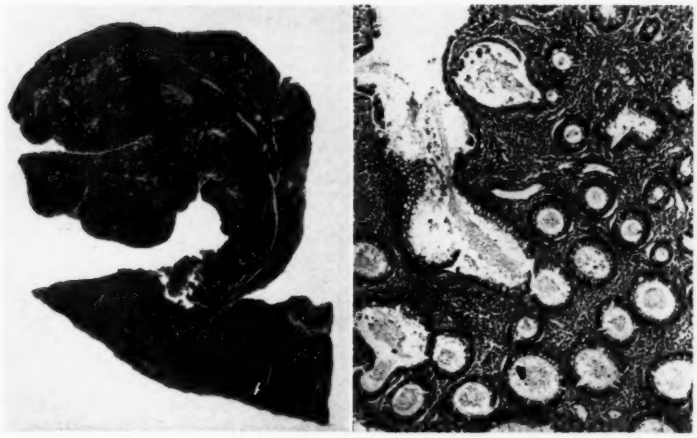


Fig. 6. a, left. Chronic ulcerative colitis; large, pedunculated pseudo-adenomatous polyp. ×36. b, Section of polyp shown in Figure 6 a in which benign regeneration is evident and large cystic glands are present. × 47.

In 34.5 per cent of the cases, presumptive evidence of a familial disposition, as indicated by a history of multiple adenomatosis or carcinoma of the colon among parents or siblings, was established. One family history deserves special mention in that both parents were found at necropsy to have multiple adenomatosis of the colon and 3 siblings died as the result of carcinoma of the large bowel, whereas one sibling died of sarcoma of the smal intestine.

In 62 per cent of the cases, the passage of blood in the stools was the chief complaint, whereas diarrhea without blood, vague abdominal pain and the protrusion of rectal polyps were noted in that order of frequency among the remainder. In 69 per cent of the cases, the polyps were distributed throughout

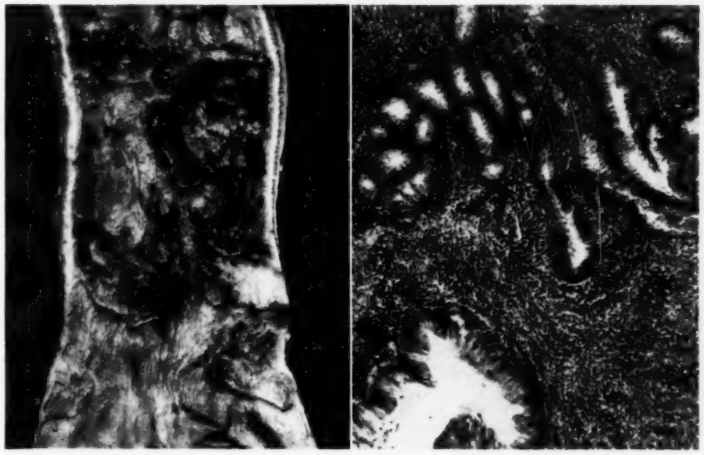


Fig. 7. a, left. Chronic ulcerative colitis; polyps; b, section of one of the polyps in a case of chronic ulcerative colitis revealing adenomatous proliferation of the glands. × 56.

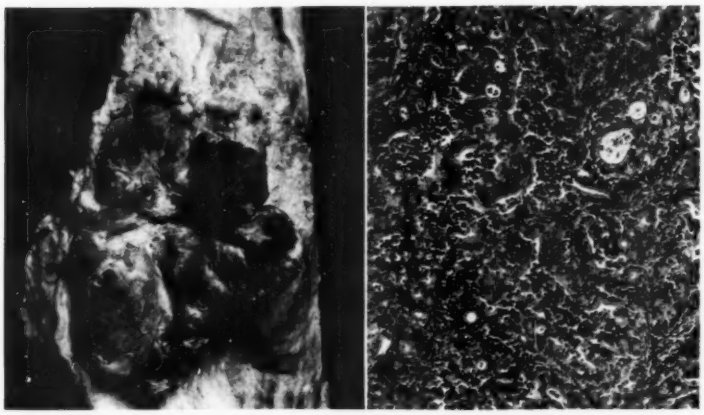


Fig. 8. a, left. Malignant polyp of the sigmoid occurring as a complication of chronic ulcerative colitis with several smaller polyps immediately proximal to the carcinoma; b, section of malignant polyp which is adenocarcinoma, grade 3. ×57.

the entire large bowel. The right side of the colon escaped involvement more frequently than the left and the rectum was free of polyps in only 2 instances. Of interest was the observation that the entire large bowel was involved in all the cases in which a familial disposition was evident. In 2 instances the lining of the stomach and entire intestinal tract was covered with polyps and, in another patient, the stomach, in addition to the colon, was the seat of polyposis. A solitary duodenal adenoma was found in 2 patients.

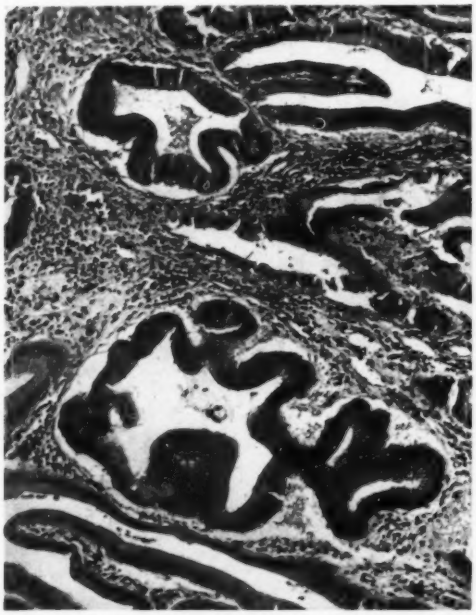


Fig. 9. Section of polyp in which carcinoma (grade 1) is seen in an adenomatous polyp. ×76.

Polyps of every conceivable variety were observed, ranging from tiny mammillations that escaped casual scrutiny to large pedunculated tumors. In some specimens countless polyps diffusely covered the surface of the opened bowel, whereas in others discrete tumors were sparsely scattered throughout. A segmental involvement was occasionally noted. The adenomatous character of the polyps was a constant finding and our interest was centered chiefly in the identification of carcinomatous changes. In pathological material from 24 cases multiple carcinoma existed. The majority were grade 1 (Broders' classification).

In order to study the pathogenesis of the polyps, numerous histological preparations were made from regions in which the mucosa appeared to be normal or in which tiny mammillations were observed. The mucosa was invariably well formed and intact, frequently exhibiting a wavy, undulating appearance. Infiltration of the interstitial tissue with

lymphoid and plasma cells was a constant finding, but in no instance was there evidence of severe destructive inflammation, as seen in cases of chronic ulcerative colitis. The muscular and serosal layers of the bowel appeared to be normal.

Localized benign hyperplasia of the glands was occasionally observed, and in some sections this appeared to be merely a lengthening of an isolated group of glands (Fig. 1). Localized adenomatous hyperplasia was most conspicuous in sections from the grossly normal mucosa. Histological sections of the tiny excrescences were usually found to be composed of a cluster of adenomatous glands. Frequently, this adenomatous change appeared to involve several isolated glands and generally it was first observed in the tips of the glands (Fig. 2). Carcinomatous changes were encountered twice in these tiny excrescences.

An observation of paramount interest in the study of the pathogenesis of the polyps was the invariable presence of hyperplastic lymph follicles in the submucosa (Fig. 3) and less frequently in the mucosa. The germinal centers of these follicles were conspicuously enlarged and contained many mitotic figures. Not infrequently, a localized bulging of the mucosa over such an enlarged follicle occurred, and, furthermore, adenomatous changes in these protruded areas were observed with striking regularity. The frequent presence of lymph follicles in the stalks of the well developed polyps might be interpreted as being a more advanced phase of this process.

Polyposis associated with chronic ulcerative colitis. Patients who had chronic ulcerative colitis and who registered at The Mayo Clinic during the period of 1913 to 1923 inclusive, will be considered under group A, whereas group B is comprised of those who entered the clinic during the period of 1932 to 1934 inclusive.

Polyps were found in 66 of 417 patients in group A (15.8 per cent). Of 400 patients in group B, polyps were demonstrated in 40 (10 per cent). In both groups the incidence of polyps was greatest in the third and fourth decades of life.

The inflammatory process had involved the entire colon in the majority of cases. The frequency with which the wall of the bowel escaped involvement varied directly with the distance from the rectum, and in both groups only 1 case was encountered in which the rectum was not involved. The severity of the chronic ulcerative colitis, as determined by the local and constitutional manifestations of the disease and by the proctoscopic and roentgenographic appearance of the bowel, was graded in group A as severe in 47 per cent, moderate in 35 per cent, and mild in 18 per cent of the cases, whereas in group B 35 per cent were graded as moderate and 28 per cent as mild. The average duration of the symptoms of colitis was 6 years in group A and 5.7 years in group B. The shortest period of symptoms was 6 weeks and the longest was 34 years.

In group A the polyps were distributed throughout the entire large bowel in 16.6 per cent of the cases, whereas in 51.5 per cent they were limited to the rectum. Comparable distribution existed in group B. The polyps were found in largest numbers in the rectum and decreased in frequency in the more proximal segments of the large intestine.

In the earlier group the polyps were demonstrated by proctoscopic examination in 85 per cent of the cases, whereas roentgenographic study of the colon revealed their presence in only 10.6 per cent. They were found at postmortem examination in 26 per cent of the cases. In group B the polyps were seen proctoscopically in 90 per cent of the cases, whereas they were demonstrated roentgenologically in only 35 per cent of cases, and in only 10 per cent were they found at postmortem examination.

In many cases the cicatricial narrowing of the bowel that invariably occurred with chronic ulcerative colitis was sufficiently exaggerated in a localized segment to constitute a stricture. When such a lesion developed, polyps were constantly found in the adjacent mucosa, usually above the strictured point and, in some instances, this was the sole site of the polyps. In group A, strictures were found in 31.8 per cent of the cases, whereas in group B such areas of narrowing were found in 20 per cent.

Of the cases in group A, 48.5 per cent were subjected to a major surgical operation, usually an ileostomy, with an immediate postoperative mortality rate of 47 per cent. Of the medically treated patients, 53.5 per cent died within a period of 4 years. Only 6 (15 per cent) of the patients in group B were treated surgically, and of these 4 died after operation. The mortality rate associated with medical treatment in this series over a period of 4 years was only 11.5 per cent.

Macroscopically, the polyps varied in size from a few millimeters to as much as 3 centimeters in diameter. In most of the specimens the polyps appeared as protruding tufts of mucosa in areas that were otherwise devoid of any mucous membrane (Fig. 4). These tags often formed bridges of mucosa and granulation tissue which were attached at both extremities to the wall of the bowel (Fig. 5). However, occasionally the polyps had the appearance of exuberant outgrowths from the already diseased mucosa, whereas in a few specimens a polypoid tumor highly suggestive of carcinoma was encountered. In all specimens the ulcerative process seemingly had damaged irreparably the wall of the bowel with great thickening and fibrosis of the submucous and muscular layers.

After examining numerous histological sections, it was decided to classify the polyps in a manner that offered some prognostic significance. Consequently they were divided into 3 groups, namely: (1) pseudo-adenomatous polyps, (2) adenomatous polyps, and (3) carcinomatous polyps.

Included in the group of pseudo-adenomatous polyps were structures ranging from small tags of granulation tissue in which there was a more or less complete absence of mucosa to large pedunculated polyps of several centimeters in diameter composed largely of hyperplastic glands (Fig. 6). However, the important criterion in this classification was not the amount of glandular tissue in the polyps but was rather the cytological structure of the individual glands. Consequently, these polyps often appeared adenomatous at first glance, but, upon more detailed scrutiny, the glandular hyperplasia was recognized as a benign regenerative process, as evidenced by the orderly arrangement of the lining cells in which the normally staining nuclei were aligned along the basement membranes with an overlying layer of clear cytoplasm. The cells secreted mucus in normal or excessive amounts. Frequently large cystic glands were seen. In other words, some of the pseudo-adenomatous polyps were very hyperplastic, but this hyperplasia was an orderly, functioning response to the underlying stimulus—inflammation. The use of the term "inflammatory" has been avoided in this classification, inasmuch as evidence of inflammation was invariably conspicuous in all the polyps associated with chronic ulcerative colitis. The term "pseudo-adenomatous" has been applied to this group in order to indicate that any evidence of a tendency toward neoplastic change was lacking. This group is analogous to the pseudopolyps as classified by Wesson and Bargen.

The second group included all polyps in which any adenomatous hyperplasia was discovered. These ranged from small finger-like projections of granulation tissue containing only a few glands to large pedunculated and sessile polyps. Usually they were of larger size and possessed a more exuberant character than the pseudo-adenomatous polyps, but exceptions to this were found. Adenomatous changes in the glands were manifested by an increase in the size, abnormally deep staining, and malalignment of the nuclei, numerous mitotic figures, diminution in the amount of cytoplasm, and diminution in the amount of mucus produced. These changes, in some instances, were slight (Fig. 7) and were distinguished only with great difficulty from the more advanced types of pseudo-adenomatous hyperplasia. On the other hand, advanced adenomatous hyperplasia constituted a fine distinction from carcinoma *in situ*. Adenomatous changes were occasionally confined to a few isolated glands in a polyp which was composed almost entirely of granulation tissue or of benign glandular elements. The cytological changes in these polyps constitute a definite type of dedifferentiation and anaplasia and represent an abnormal regenerative response. It is a matter of interesting conjecture as to whether these polyps would even-

tually become carcinomatous if the individuals lived sufficiently long, but it seems obvious that the tendency toward malignant change in these is increased. These polyps are similar in cytological details to the adenomas associated with multiple polyposis and those designated as true polyps by Wesson and Bargen.

Carcinomatous polyps were usually of relatively large size, and they presented a dusky red, hemorrhagic appearance which immediately aroused a suspicion of their malignant nature (Fig. 8). However, in several instances carcinoma *in situ* was discovered in small adenomatous polyps (Fig. 9). This distinction between an advanced adenomatous change and carcinoma of low grade frequently was barely perceptible and was evidenced by more advanced dedifferentiation and anaplasia, and occasionally by invasion of the submucosa.

Pathological material from 32 of the cases was available, being secured at necropsy in 20 cases, by biopsy during proctoscopic examination in 8 cases, and as a surgical specimen in 4 cases. In 18 (56.2 per cent) of the cases, the polyps were classified as pseudo-adenomatous. Adenomatous polyps were found in 7 (21.9 per cent) of the cases, the adenomatous changes being slight in 4 and severe in 3 instances. Carcinomatous changes were identified in 7 (21.9 per cent) of the cases, and 3 were grade 1, 1 was grade 2, whereas 2 were grade 3. In one specimen 2 polyps were carcinoma grade 1 and 2 others were grade 3. In 3 of these cases multiple carcinoma was found, whereas in 2 specimens other polyps showed adenomatous changes. Of the carcinomatous polyps 2 were papillary in structure. In 2 cases carcinoma *in situ* was discovered.

SUMMARY AND CONCLUSIONS

1. A comparative clinicopathological study of a group of cases of multiple adenomatosis and of polyposis, occurring in the course of chronic ulcerative colitis, revealed that these 2 conditions are extremely dissimilar both clinically and pathologically. Changes were apparent in the clinical course of the 2 conditions as well as in their histogenetic and pathological characteristics.

2. In the cases of multiple adenomatosis the onset of symptoms was insidious with rarely more trouble than that caused by passing an increasing amount of blood by rectum. Rarely, except in late stages of the condition, was the individual ill in any clinical sense. In the cases of polyposis associated with chronic ulcerative colitis the onset of symptoms was likely to be insidious and the illness itself was much more likely to be of a severe fulminating type. If this was not apparent at the onset, such a condition prevailed at some time during the course of the disease and before polyposis became the important difficulty.

3. A heredofamilial disposition existed in 34.5 per cent of the cases of multiple adenomatosis. This entity is essentially a disease of youth, as approximately two-thirds of the cases in this study occurred during the first 3 decades of life. Multiple adenomatosis often developed in the later decades of life and this type is indistinguishable pathologically and clinically from that occurring in adolescence.

4. The individual lesion consisted of a primary epithelial change attended by minimal evidence of inflammation. Hypertrophic lymph follicles seemed to play a rôle in the pathogenesis of these polyps.

5. The condition is characterized by the occurrence of myriads of true adenomatous polyps in which carcinomatous changes were found in 62.5 per cent of the cases, and in 25 per cent there were multiple carcinomas.

6. Studies of the pathogenesis of the multiple adenomas revealed that multiple small foci of adenomatous proliferation develop in a usually hyperplastic mucosa. Consequently, multiple adenomatosis is a disease of the entire mucosa, and therapy which eradicates only the existent polyps fails to cure the condition. Regions of benign hyperplasia are frequently observed. Conspicuous hyperplastic lymph follicles, which may be the result of subclinical inflammation, are frequently present. Their relation to the pathogenesis of the polyps may be of great importance.

7. Polyposis arising as a complication of chronic ulcerative colitis is characterized by widespread inflammation and destruction of the mucosa with inflammatory involvement

of the entire wall of the bowel. The polyps are composed of tufts of granulation tissue and of surviving remnants of mucosa in most of which benign regenerative hyperplasia is evident and, in many of which, true adenomatous, and even carcinomatous proliferation ensues. Consequently, these polyps were classified as (1) pseudo-adenomatous, (2) adenomatous, and (3) carcinomatous. The relative incidence of these types of polyposis associated with chronic ulcerative colitis and with multiple adenomatosis is: Of the multiple adenomatosis group, 100 per cent were adenomatous and of these 62.5 per cent were carcinomatous; of the chronic ulcerative colitis group, 56.2 per cent were pseudo-adenomatous, 21.9 were adenomatous, and 21.9 per cent were carcinomatous.

8. The comparative study of polyposis complicating chronic ulcerative colitis in groups A and B revealed several significant facts. The relative incidence of polyps in group B was only 10 per cent as compared with an incidence of 15.8 per cent in group A. Inasmuch as it has been shown that the incidence increased with the severity of the disease, this decreased incidence of polyps is more than likely attributable to improvements in the modern therapeusis of chronic ulcerative colitis. Improvement in roentgenological diagnosis was apparent in the fact that the polyps were demonstrated by roentgenological means in 35 per cent of the cases in the more recent group as compared to 10.6 per cent in the former. Surgical treatment was resorted to in 48.5 per cent of the earlier cases with an attendant mortality rate of 47 per cent, whereas in the more recent group surgical procedures were used in only 15 per cent of the cases with a mortality rate of 66 per cent.

9. Polyps associated with chronic ulcerative colitis seem to be the result of widespread ulceration and destruction of the mucosa, associated with remaining islets of inflammatory mucous membrane, and followed by cicatricial distortion of the damaged lining of the bowel. The resulting polyps were predominantly pseudo-adenomatous (56 per cent), although adenomatous changes were observed in 21.9 per cent. Carcinoma in these cases occurred with similar frequency (21.9 per cent).

10. It seems obvious, therefore, that from the standpoint of the probability of the development of carcinoma, multiple adenomatosis is potentially a much more dangerous disease than polyposis associated with chronic ulcerative colitis.

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TETANUS AT THE JOHN SEALY HOSPITAL

Observations upon the Distribution of Tetanus throughout the United States

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DURING the period 1905 to 1938 there have been 102 cases of tetanus treated on the surgical service of the John Sealy Hospital, Galveston, and locally it has become a belief that tetanus is peculiarly common in this vicinity. Recently, while reviewing these cases, we have taken occasion to inquire into the distribution of tetanus throughout the United States. The annual mortality statistics report of the Bureau of Census enumerates the deaths from tetanus in each state of the registration area but supplies the death rate per 100,000 population only for the area as a whole. Using the enumeration of deaths and the Bureau's annual estimation of populations, we have computed the death rate from tetanus per million population for each state and for each year of the period 1923 to 1935. Certain of the data thus obtained are sufficiently informative to merit presentation at this time in conjunction with a report of the experience with tetanus at the John Sealy Hospital.

GEOGRAPHIC DISTRIBUTION OF TETANUS

Gessner (1918), Graffagnino and Davidson (1924), Graves (1930), and Boyce and McFetridge (1935) have reported 998 cases of tetanus treated at the New Orleans Charity Hospital during the period 1906 to 1934, whereas 90 patients were treated in the John Sealy Hospital during these years. Thus Charity Hospital encountered 11 times as many cases during a period in which the population of New Orleans averaged 8.6 times that of Galveston. Apparently tetanus is equally as common in New Orleans. There is no doubt but that the disease is more prevalent both in Galveston and in New Orleans than in the cities of the North. In 1937 Huntington, Thompson, and Gordon were able to collect only 642 cases from the records of 18 hospitals situated in the northeastern quarter of the United States. These hospitals totalled about 10,000 beds and a number of the cases occurred prior to 1905. In comparison, the Charity Hospital and the John Sealy Hospital, having a combined capacity of less than 2,200 beds, have treated over 1,100 patients with tetanus since 1905. It is obvious that tetanus occurs more commonly in the Gulf Coast region than in the northeastern section of the country.

To obtain a more satisfactory estimate of the geographic distribution of the disease we have constructed the map shown in Figure 1 from data compiled from the *Mortality Statistics of the Bureau of Census*. The years 1933, 1934, and 1935 were chosen because the reports for these years are the only ones available which include Texas, this state not having joined the registration area until 1933. The map shows that deaths from tetanus are much more common in the southern states and particularly in those states bordering upon the Gulf.

A study of the literature reveals that for tetanus the mortality rate in treated patients has been fairly uniform throughout the country. Therefore, *in the absence of dependable figures bearing directly upon the incidence of tetanus, we feel justified in assuming that the data upon deaths from the disease presented in Figure 1 can be considered a fair index of the geographic incidence of tetanus.*[1]

Factors explaining the geographic distribution. A high incidence of tetanus has ordinarily been considered an accompaniment

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[1]As will be shown later, the number of deaths is not necessarily a good index of the incidence in states having a large negro population.

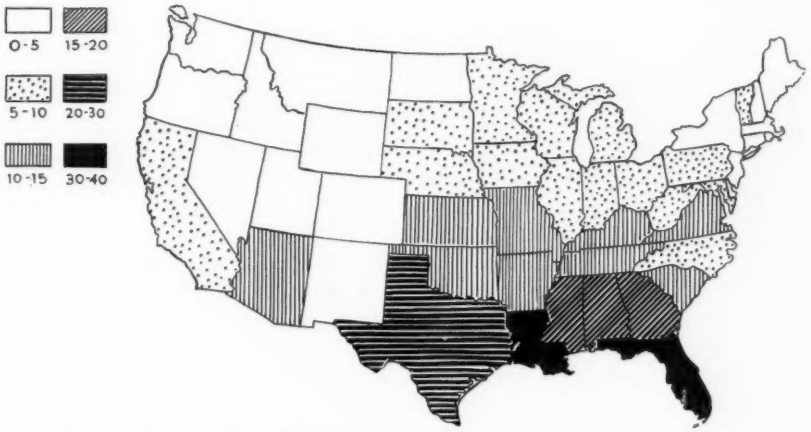


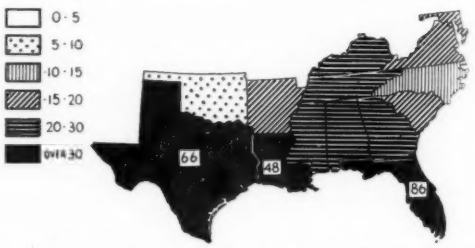
Fig. 1. Average annual deaths from tetanus per million population based upon the years 1933, 1934, and 1935 and the official 1930 populations.

of intensive cultivation and fertilization of the soil. However, it is impossible to account for the findings shown in Figure 1 solely by soil culture. The relatively low incidence in the midwestern farming states and in the old cultivated states of the northeast defies explanation on this basis. Other factors must be considered: (1) The influence of climate upon the growth of tetanus bacilli in the soil; (2) a difference in the susceptibility of the population, particularly with reference to the large negro population in the states bordering upon the Gulf; (3) the outdoor life throughout the year in the most southern regions together with the custom that many people have of going without shoes; and (4) ineffective treatment of wounds and failure to use antitoxin in prophylaxis in the areas where tetanus is prevalent.

Although the high incidence of tetanus in the Gulf States may depend in part upon the character of the soil, climatic factors must be important. High mean annual temperature, absence of winter freezing, copious rainfall, and great humidity possibly combine to favor the growth of the bacillus in the soil. If the great prevalence in the Gulf Coast region is conditioned by this subtropical, maritime climate there should be a sharp contrast between the incidence in the coastal plains of Texas and that in the higher, drier portions of the state. The State Department of Health has been unable to furnish data for us to make this comparison, but through city health officers we have obtained information which permits a comparison of 5 cities of the state over an 11 year period. During the years 1927 to 1937 the average annual deaths from tetanus expressed as deaths per million population were as follows: Galveston, 32; Houston, 22; Fort Worth, 21; El Paso, 15; and San Antonio, 41.

The low rate in El Paso is in line with its warm but dry climate. The city, which lies at an elevation of nearly 4,000 feet, has an annual rainfall of only 9 inches. Furthermore, the city is not an agricultural center. On the other hand the high rate in San Antonio is somewhat perplexing. Although this city is warm it has a much drier climate than either Galveston or Houston, a fact demonstrating that the distribution of tetanus in Texas cannot be entirely a function of the rainfall. San Antonio, however, does lie in a farming region and the population includes a considerable proportion of Mexicans of the laboring class who are notorious for their unhygienic mode of life and reluctance to seek medical care.

For those states having a large negro population the Bureau of Census in its Mortality Statistics separates the negro and white populations. Consequently it has been possible to



Figs. 2 and 3. Comparison of tetanus death rates for white and negro populations based upon the years 1933, 1934, and 1935 and the official 1930 populations. Figure 2 shows the average annual deaths from tetanus among the white population of 14 southern states. Figure 3 shows the average annual deaths from tetanus among the negro population of 14 southern states. The death rate is higher for negroes except in Oklahoma.

prepare Figure 2, mapping the deaths from tetanus in the south on the basis of white population alone. Comparing the shading in this map with that in Figure 1 it is apparent that the death rate from tetanus in whites has not been particularly high except in the states of Florida, Louisiana, and Texas. In these 3 states the rate has exceeded that elsewhere in the country, again suggesting a climatic factor.

Figure 3 shows the death rates from tetanus among the negro population in the south. In every state but Oklahoma the rate has been higher for negroes than for whites and in many states the difference is startling. In the absence of adequate data bearing directly upon the morbidity it is impossible to state whether the high death rate among negroes is due to a greater incidence of the disease or to a higher mortality. It would seem safe to presume that both factors play a part. The great majority of negroes in the South are engaged in manual pursuits. Soil contamination of wounds must be a common occurrence, particularly in view of the practice of going barefooted. Inadequate care of wounds and failure to use antitoxin in prophylaxis would result in a high incidence of tetanus. Once the disease is contracted, delay or failure in receiving medical attention would lead to a high mortality.

The view that the high death rate in negroes is due to such factors rather than to a racial susceptibility is strengthened by the experience in Galveston where the John Sealy Hospital has offered the colored population free and adequate treatment of wounds. During the past 15 years exactly one-third of tetanus deaths in Galveston have been in negroes whereas the negroes have constituted one-fourth of the population (25.2 per cent in 1929). This slight disparity might reasonably be explained on an occupational basis. At the John Sealy Hospital over a 15 year period negroes constituted 32 per cent of admissions and 33 per cent of tetanus cases. In our series of 102 cases of tetanus the mortality among negro patients was 44.1 per cent as compared to 52.9 per cent among white patients. These figures argue against any significant racial susceptibility to tetanus. Consequently it is our belief that the death rate from tetanus in the South is higher among negroes because the negroes are engaged in manual pursuits in much greater proportion and they are under social and economic conditions which deny them effective prophylaxis as well as adequate treatment for the disease.

The trend in the death rate from tetanus. For the Registration Area as a whole there were 17 tetanus deaths per million population in 1923. This figure had decreased to 8 deaths per million by 1935. In 1923 among infectious and parasitic diseases tetanus ranked thirteenth in importance as a cause of death. In 1935 it was still thirteenth. Thus progress in prevention of fatal tetanus has kept pace with that in prevention of other infectious disease. Throughout this period there was a decrease in the tetanus death rate in every state but Idaho where a very low rate remained practically unchanged.

Figure 4 illustrates the trend in the death rate from tetanus for the negro population. The heavy line indicates the death rate for the entire population of the United States

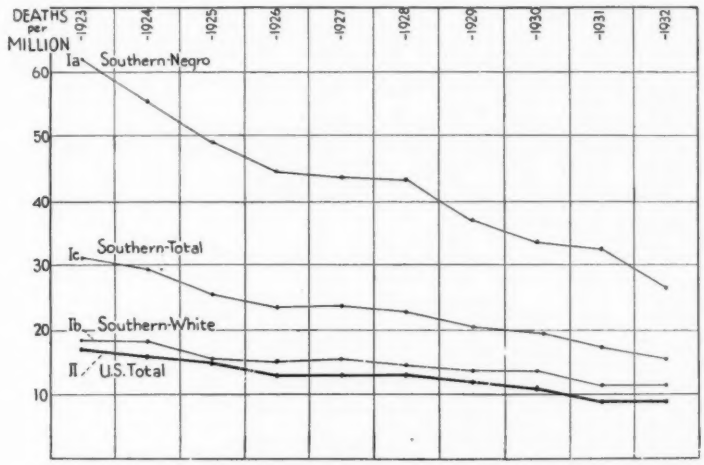


Fig. 4. Trend in death rate from tetanus for the 10 year period 1923 to 1932. Ia., southern negro; Ib., southern white; Ic., southern total; II., entire U. S. Registration Area.

registration area for the years 1923 to 1932. Comparable curves are shown for the negro, white, and total populations of the 9 southern states which were in the area throughout this period.[1] It is seen that there was a relatively greater decrease in tetanus deaths among the southern negroes than among the southern whites or among the entire population of all the registered states. This very favorable trend affecting the source of the highest mortality is further emphasized when one compares the death rate curve for the registration area as a whole with curves for the 3 states showing the highest rates in Figures 2 and 3. Thus, while the tetanus death rate for the entire area decreased from 17 per million in 1923 to 8 per million in 1935, the rate for Florida decreased from 64 to 32 and that for Louisiana dropped from 94 to 27.5. Unofficial figures indicate a similar decrease in Texas. Again it is seen that the greatest improvement has occurred in the areas where it was most needed. Nevertheless, it is in these regions that tetanus is still most prevalent.

TETANUS AT THE JOHN SEALY HOSPITAL

1. Incidence. In our judgment the high incidence of tetanus in Galveston has depended upon a soil rich in tetanus bacilli. The city was built upon a sand bar in the Gulf of Mexico and intensive fertilization has been practiced throughout the 100 years of its existence. Furthermore, the climate is warm and very moist. Outdoor sports are popular throughout the year. We believe that other causes of a high incidence of tetanus are not important locally. The disease is feared and physicians treat wounds radically and give antitoxin routinely. In the presence of an effective free clinic a large negro population has not materially increased the tetanus rate. Although many children go barefooted, wounds about the foot have accounted for less than one-third of our cases and for only 15 of 41 patients under 14 years of age. In view of these considerations it would seem that the prevalence of tetanus is largely a reflection of the climate and of the soil.

Incidence in relation to race, sex, and age. Whereas negro patients comprised 32 per cent of the John Sealy Hospital admissions (1920 to 1935), they constituted 33 per cent of the 102 cases of tetanus treated. Although the local population is only 25 per cent negro, this disparity might be predicted upon an occupational basis alone. Thirty-six and two-tenths per cent of the 102 cases of tetanus were female patients. Charity Hospital re-

[1]Florida, Kentucky, Louisiana, Maryland, Mississippi, North Carolina, South Carolina, Tennessee, and Virginia.

TABLE I.—INCIDENCE OF TETANUS AT THE JOHN SEALY HOSPITAL

Classification	Cases number	Mortality per cent
Entire series	102	50.0
Race:		
White	68	52.9
Negro	34	44.1
Sex:		
Male	63	52.4
Female	39	46.2
Age in years:		
1–10	30	46.6
10–20	15	46.6
20–30	19	42.1
30–40	14	57.1
40–50	12	66.6
50–60	5	20.0
60–70	2	50.0
70–80	1	100.0
Site of wound:		
Lower extremity	40	32.5
Upper extremity	24	62.5
Head and neck	3	66.6
Internal (criminal abortion, operation)	20	55.0
Type of wound:		
Puncture wound	31	35.5
Blank-pistol wound	4	75.0
Other accidental wound	20	50.0
Smallpox vaccination	10	70.0
Hypodermic wound in drug addict	4	75.0
Chronic leg ulcer	3	0.0
Criminal abortion	17	52.9
Surgical operation	3	66.6

ported that 37.3 per cent of their tetanus patients were female (3). When the cases arising from criminal abortion, vaccination, surgical operation, etc., are excluded, one finds that only 19.6 per cent of the cases arising from accidental wounds were female patients. Presumably this figure signifies the low proportion of traumatic wounds occurring in female subjects. In 98 of the 102 cases the age was recorded. The distribution in relation to decades is shown in Table I. The great incidence during the first decade of life and the low incidence in persons past 50 years is attributed chiefly to differences in habit and in activity although a difference in susceptibility also may exist. Of the 30 cases in persons less than 10 years of age 10 were due to puncture wounds of the foot and 5 to smallpox vaccination wounds.

Incidence in relation to site and type of wound. Table I shows the portal of entry of the tetanus bacillus in 92 cases. In the other 10 cases the wound was unknown. Although a puncture wound was the commonest cause, in 15 instances the disease arose from a laceration. The 10 cases resulting from infected vaccination wounds were scattered through the years 1914 to 1929, 3 of the cases occurring in 1925. The cases which arose from surgical operations followed the removal of a gangrenous appendix in 2 instances and an accidental tear of the ileum repaired at operation in the other instance.

Incidence in relation to the prophylactic use of tetanus antitoxin. Although there is no doubt that the prophylactic use of tetanus antitoxin has done much to decrease the incidence of tetanus, it is generally known that the disease can occur in patients who have been administered the serum for prophylaxis. The Charity Hospital reported 15 such cases with 9 fatalities (3). We know of 2 such cases in our series. In 1936, a child developed fatal tetanus 4 days after receiving 3,000 units of antitoxin. In 1937, an adult diabetic developed tetanus 12 days after suffering a compound dislocation of a toe resulting in gangrene of the foot but only 3 days after receiving 3,000 units of antitoxin. She recovered after amputation of the leg.

It is generally stated that antitoxin remains in the blood stream for less than 10 days and for this reason the United States Army requires that a second dose be administered after 1 week. In view of the impression that if in rare cases the antitoxin does not prevent the disease it at least delays it, it is important to note that both of the cases cited developed within the first week after serum prophylaxis.

2. *Mortality.* One hundred and two patients with tetanus were treated at the John Sealy Hospital during the period 1905 to 1938. A few cases, so mild as to be doubtful, have not been included in the series and several cases of babies with tetanus neonatorum treated on the gynecological service have been omitted. Otherwise the study includes all tetanus diagnosed during this period. Since the value of tetanus antitoxin was demonstrated by von Behring in 1890, the serum coming into general use a few years later, this entire series falls within the antitoxin era, every case receiving at least a small amount of antitoxin.

The mortality for the entire series of 102 cases was exactly 50 per cent. In Table II

this mortality is compared with that reported by certain other hospitals for approximately the same period of years. The table shows that the local mortality was lower, and, from a statistical standpoint, significantly lower. In view of our limited number of cases, however, it is possible that the difference is only apparent. The decrease in mortality during recent years is discussed elsewhere.

Mortality in relation to race, sex and age. In this hospital a slightly higher mortality was observed in white patients than in negroes but the difference is not sufficient to be significant (Table II). Boyce and McFetridge in 1935 reported that in New Orleans the mortality was greater among the blacks. This they blame upon a tendency of the southern negro to delay medical consultation. It is true that in the Galveston series there has been some indication of such a delay, only 39 per cent of the negro patients having entered the hospital during the first 2 days of the disease as compared with 60 per cent of the whites. In spite of this delay a lower mortality was observed in the negroes which is surprising. Evidence will be presented, however, to indicate that most cases of tetanus which delay medical consultation unduly are mild cases of the disease.

As shown in Table II there was no significant difference between the mortality in male and that in female patients. With respect to the influence of age our series does not permit an accurate appraisal, the number of cases in the upper age brackets being too small (Table I). By dividing the patients into 2 age groups (Table II), a somewhat higher rate was suggested for patients over 40.

Mortality in relation to incubation period. It has been a rather general belief that the cases of tetanus developing after a short incubation period are apt to be more serious. However, from experience at the Charity Hospital, Boyce and McFetridge (1935) state that "the relationship between incubation period and mortality rate is a tendency rather than a fact." Huntington, Thompson, and Gordon (1937) conclude that a rapid progression of symptoms after the onset is a more reliable index of grave prognosis than is a short incubation period. Observations in our series tend to corroborate this opinion. As shown in Table II a higher mortality rate was observed in the cases in which the incubation period was longer. Although the difference observed was not sufficient to warrant the conclusion that a short period is favorable, it does suffice to indicate that in any given case an accurate prognosis cannot be based upon the length of the incubation period. Furthermore, it is well to stress that in many cases the incubation period which one can calculate is only an apparent incubation period and is not necessarily the true one.

Mortality in relation to duration of symptoms prior to hospital admission. As shown in Table II it was possible to calculate the day of the disease upon which the patient sought hospitalization in 84 of the 102 cases. The mortality was so much greater among those

TABLE II.—STATISTICAL STUDY OF MORTALITY IN TETANUS TREATED AT THE JOHN SEALY HOSPITAL

Classification	Cases number[1]	Mortality per cent	Difference in mortality per cent	Chi square	Approximate probability per cent[2]
Race:					
White	68	52.9			
Negro	34	44.1	8.8	0.71	40
Sex:					
Male	63	52.4			
Female	39	46.2	6.2	0.37	55
Age in years:					
Under 40	78	47.4			
Over 40	20	55.0	7.6	0.36	55
Site of wound:					
Lower extremity	40	32.5			
Upper extremity	24	62.5	30.0	5.49	2
Incubation period:					
5 days or less	12	25.0			
More than 5 days	58	50.0	25.0	2.50	11
10 days or less	45	44.4			
More than 10 days	25	48.0	3.6	0.08	78
Day of disease admitted:					
Third day or before	61	57.3			
After third day	23	21.7	35.6	8.50	0.3
Trend in mortality:					
First 75 cases	75	58.7			
Last 27 cases	27	25.9	32.8	8.51	0.3

[1]There were 102 cases at the John Sealy Hospital and the mortality was 50 per cent. There were 1,568 cases from other selected hospitals. This figure has been compiled from the 4 reports upon tetanus at the Charity Hospital, New Orleans, and from Huntington, Thompson and Gordon's collection of cases from 18 hospitals in the northeastern quarter of the United States. Mortality in this group was 62.7 per cent; difference in mortality, 12.7 per cent; chi square, 6.54; approximate probability, 1 per cent.

[2]The figure given represents the approximate probability that the difference observed in the mortality is due merely to chance. Ordinarily values below 5 per cent are suggestive of significance whereas 1 per cent is considered strongly indicative of significance.

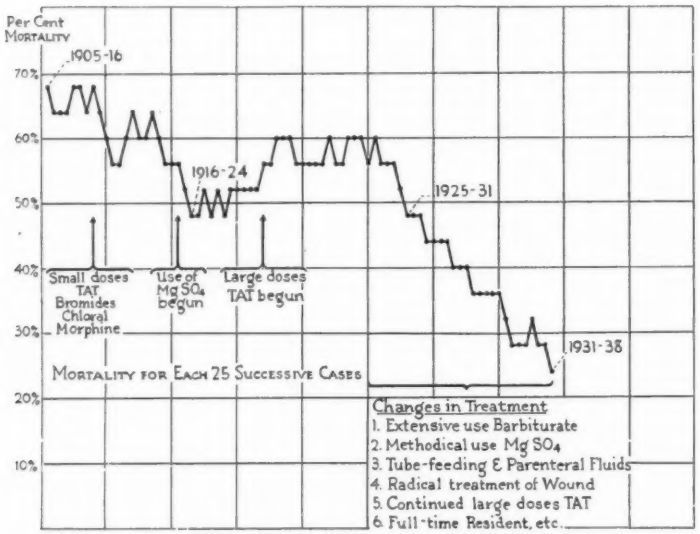


Fig. 5. Correlation of mortality in tetanus with treatment based upon 102 cases treated at the John Sealy Hospital. The 78 points on the curve represent the percentage mortality in each series of 25 successive cases, beginning with Cases 1 to 25 at the left, followed by Cases 2 to 26, 3 to 27, etc., to end with Cases 78 to 102 at extreme right.

entering during the first 3 days of the disease that its significance cannot be questioned. This finding confirms the opinion of Huntington, Thompson, and Gordon (1937) that a rapid progression of symptoms is a bad omen in tetanus and that "patients whose symptoms compel them to seek hospitalization within 24 hours of the onset of the disease are patients with severe tetanus." The experience in Galveston has led us to conclude that tetanus which becomes marked within 48 hours of the first prodromal symptom is very serious. Furthermore, we believe that in any case of tetanus a forecast should be withheld until the response to 24 hours of hospital treatment has been determined.

Mortality in relation to treatment. In studying our series of 102 cases of tetanus it immediately became apparent that during recent years the mortality has been lower. A very significant difference between the rate for the first three-quarters of the series and that for the last one-quarter is shown in Table II. We have no reason to believe that the lowered mortality indicates a milder form of the disease. Many of the recent cases have been severe but a number which seemed hopeless have recovered. For this reason the records have been studied carefully in an attempt to correlate the lowering of mortality rate with changes in the treatment.

To picture the trend in the mortality in tetanus in this hospital since 1905 we have numbered the 102 cases in order of hospitalization and have determined the percentage mortality for each of the possible 78 series of 25 successive cases. These mortality figures are plotted to form a horizontal curve in Figure 5, beginning with Cases 1 to 25 at the first point on the left, followed by Cases 2 to 26 and so on to terminate with Cases 78 to 102 at the extreme right. It is evident that since 1925 there has been a continuous and progressive lowering of the mortality rate below any previous figure until for the last 25 cases there have been only 6 deaths as compared to 19 recoveries, a mortality of 24 per cent. It is our belief that this result must be attributed to improvements in therapy. A chronological survey will show this.

Prior to 1920 no patient received in treatment as much as 50,000 units of antitoxin. For sedation one depended entirely upon chloral hydrate and bromides with occasional hypodermics of morphine. The causative wound was sometimes excised and in other instances was simply cauterized with phenol. During this period the mortality rate was high. In 1916, following the work of Meltzer, the hypodermic use of 25 per cent magnesium sulphate was introduced in the hope that it would aid in relieving spasm. For a number of years, however, it was given in a hit-or-miss fashion so that the drug did not receive a fair trial. In 1920 the dosage of antitoxin was greatly increased and since that time the total amount administered to patients recovering from the disease has averaged 140,000 units. Nevertheless, in spite of this change, the mortality rate remained high until 1926.

In contrasting the treatment during the past 10 or 12 years some points require mention:

1. Barbiturates, particularly luminal, sodium luminal, and sodium amytal, have served as the chief sedatives. Chloral hydrate is still used in some cases. Our experience with avertin is too slight to warrant an opinion.[1]

2. Magnesium sulphate in 25 per cent solution has been given intramuscularly or subcutaneously in 2 to 6 cubic centimeter doses and repeated each 4 hours as long as it has seemed needed. We believe that in many cases this methodical use of the drug has been a valuable adjunct in relaxing spasm.

The use of barbiturates and of magnesium sulphate, both in huge doses, is founded upon the belief that the patient with tetanus is benefited if muscular rigidity is relieved. In most instances this combination of drugs has produced muscular relaxation and has also prevented clonic disturbances. In view of the work of Abel, Hampil and Jonas in 1935 and that of Firor and Lamont in 1938, suggesting that the rigidity of tetanus is a result of the action of the toxin upon voluntary muscle whereas the clonic spasms arise as a central nervous effect, it is of interest to recall that although the action of barbiturates is largely upon the central nervous system magnesium sulphate has been shown to depress irritability in living cells of all types (10).

3. A great deal of effort has been directed toward maintaining the patient's caloric and fluid requirements. In severe cases this has meant high caloric feedings through a retained nasal catheter in conjunction with saline hypodermoclysis twice daily.

4. Whenever possible the external causative wound has been subjected to radical débridement immediately upon admission. Whether such wound excision influences the course of tetanus once the disease has developed is open to question. To us it has seemed rational to remove the necrotic tissue and to establish aerobic conditions.

5. The use of large doses of tetanus antitoxin has been continued. We feel that the patient with tetanus needs every possible chance if he is to recover and we have been unwilling to dispense with antitoxin although many are questioning its therapeutic value.

6. The period under consideration has marked the addition to the surgical staff of full-time men including resident and assistant resident. The constant presence of highly trained men has meant that the patient can be watched very closely. We recall instances in which such men have spent hours at the bed of a patient and have literally refused to give up the fight.

A recent case may be cited as an example of heroic use of drugs and constant attention of the house staff:

A white male, aged 25, entered with severe tetanus on the second day of the disease and after an incubation period of 5 days. First, the puncture wound of the foot was treated radically. During the active stage of the disease tube feeding was maintained while saline and 5 per cent glucose was administered by hypodermoclysis. The patient received 78 grains of sodium luminal during the first 3 days and 800 grains of chloral hydrate thereafter. In addition he was given 1,698 cubic centimeters of 25 per cent magnesium sulphate by 4 cubic centimeter hypodermic injections and numerous doses of sodium amytal and morphine sulphate. A total of 315,000 units of tetanus antitoxin was administered. Until relaxation was secured frequent convulsions required etherization. For some days his condition appeared hopeless but the house staff were untiring in their efforts and the patient survived. It is our experience that such patients usually die when the care is relegated to the nurses and directed by standing orders.

[1]We have had no experience with the intravenous phenol treatment used so successfully by Beall (1924) or with the atropine-antitoxin and urotropin-antitoxin methods cited by Dejou (1938).

SUMMARY

In the absence of data bearing directly upon the incidence of tetanus the data upon deaths from tetanus supplied by the *Mortality Statistics of the Bureau of Census* can be used as an index to the geographic distribution of the disease. Although the tetanus death rate for the United States has been reduced by one-half during the last 15 years, the disease still causes over 1,000 deaths annually. Maps are presented (Figs. 1, 2, and 3) which illustrate that tetanus deaths are relatively much more common in the southern states where an excessively high mortality occurs in the negro population. From local experience in Galveston it is concluded that this high death rate from tetanus among southern negroes results from social, economic, and occupational influences rather than from any racial susceptibility. A promising trend is seen in that recent years have witnessed a decrease in the tetanus death rate for southern negroes which is even greater than the decrease for southern whites or for the entire population of the Registration Area (Fig. 4).

The death rate from tetanus for the southern white population is excessive only in those states having long coastal borders on the Gulf of Mexico, namely, in Florida, Louisiana, and Texas. In regard to these states the possible effect of their moist subtropical climate is discussed. As regards Galveston, where an effective free clinic has resulted in rates approximately equal for blacks and whites, it is felt that the high incidence has been primarily a reflection of the effects of long continued fertilization and a warm, moist climate in favoring the growth of tetanus bacilli in the soil.

During the period 1905 to 1938 the incidence of tetanus at the John Sealy Hospital was 0.83 case for each 1,000 hospital admissions. One hundred and two cases are listed according to race, sex, age, and cause in Table I. As shown in Table II the mortality was higher in cases arising from wounds of the upper extremity. There was no evidence that a short incubation period was of grave prognosis; on the contrary the mortality was actually greater in cases in which the incubation period exceeded 5 days. It was found, however, that the mortality was significantly higher among those patients whose symptoms compelled them to seek hospitalization during the first 3 days of the disease than among those entering later in their illness. Apparently, a rapid progression of symptoms is the bad omen in tetanus.

The mortality rate for the entire John Sealy Hospital series was exactly 50 per cent. This figure is significantly lower than that found in other reports (Table II). Furthermore, a decrease in mortality to 24 per cent for the last 25 cases (6 deaths and 19 recoveries) is shown in Figure 5. An attempt to correlate this lowering of mortality with changes in treatment has been made. It is concluded that in the past the mortality rate in tetanus often has been excessive and that a great lowering of mortality can be brought about through the energetic application of simple therapeutic measures available in any general hospital.

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RESULTS OF ATTEMPTED INDUCTION OF LABOR WITH ESTRIN

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THE cause of the onset of labor has been postulated by many investigators. However, in recent years, with a clearer understanding of the hormone blood levels, both in the pregnant and non-pregnant state, the rôle of sex hormones has become significant. Since pregnancy is a physiological state bordering on the pathological, in which the hormone balance is necessarily a delicate one, any imbalance might result in a disturbance in the organ which contains the gestation. With experimental knowledge of this fact, a few investigators have attempted to empty the uterus, both early as well as late in pregnancy. Animal experimentation has naturally been more widespread than human. Based on the complicating reports in the literature relative to the effectiveness of estrin in terminating pregnancy, we have undertaken this study.

A sufficient amount of experimental work has been carried out by various observers to substantiate the fact that uterine motility and contractility can be initiated and maintained by estrin. Whether or not these contractions are induced by the direct action of estrin or indirectly by sensitizing the uterus to the action of pituitrin is a debatable point. More credence was given to the latter view at the time Bourne and Burn (3) showed that when a uterus of a guinea pig was isolated and first treated with estrin, its contractions following addition of pituitrin were twice as great as without previous treatment with estrin. Subsequently (4) these investigators withdrew this opinion. It is known (18), however, that pregnant rats, rabbits, and cats with the pars posterior and pars intermedia of the hypophysis removed, experience labor in the normal manner. In addition, Reynolds and Firor (19) have demonstrated that estrin exerts its effect upon the rhythmic motility and uterine activity in the completely hypophysectomized rabbit in the same low dosage as in the intact animal.

It has been shown that rhythmic uterine contractions can be induced by estrin in certain animals during pregnancy, so that the products of conception may be expelled. This has been demonstrated by several investigators. Parkes and Bellerby (15) found that they could produce abortion in mice by the injection of estrin early in pregnancy. However, as pregnancy advanced, the dosage of estrin necessary to terminate the pregnancy increased. Kelly produced abortion in the guinea pig by estrin at varying stages of pregnancy. In the unanesthetized rabbit Reynolds and Firor (20) found that the uterus is refractory to the motility inducing action of theelin until the twenty-sixth day of pregnancy, but on the twenty-seventh day the injection of theelin leads to abortion and death. D'Amour and Gustavson claim to have terminated pregnancy in the rat by estrin administration and other successful interruptions have been reported in mice by Aschheim and Zondek, Fraenkel and Fels, and in rats by M. Smith.

It has been shown that the estrin level in the human rises in the latter part of pregnancy, which suggests its possible utilization in association with the onset of labor at term. The increase in the concentration of this hormone toward the end of pregnancy has been demonstrated independently by different observers. Thus Smith and Smith (24) have shown during normal pregnancy an increase of estrin from the fourth month on, with a rapid rise during the last trimester. Runge, Hartman, and Sievers have also found a sharp increase in estrin production and excretion in the few weeks preceding parturition. An ab-

From the Obstetrical Service of Cumberland Hospital.

normal rise of blood and urine levels of estrin for some time preceding spontaneous abortion in the human has been reported by Jeffcoate. Cohen, Marrian, and Watson have shown an increased urinary output of estrin just before labor. In addition, Zondek demonstrated a rise in estrin production during gestation, which is at its highest level at the time of parturition. Knaus also states that the production of estrous hormone increases as pregnancy advances while the anterior pituitary hormone production decreases. Accompanying this, there is a gradual degeneration of the corpus luteum with an increased susceptibility of the highly contractile uterine musculature to the action of posterior pituitary secretion. Collectively, these reports point toward the probable significance of the rôle of estrin in the onset of labor.

One may question the importance of increased estrin levels inasmuch as Møller-Christensen and Pedersen-Bjergaard believe that there is no difference between estrin production during childbearing in women who have normal labors and in women who have primary inertia uteri. In addition, Bourne and Bell (2) failed to induce uterine contractions in the human by massive doses of estrin. They feel that estrin probably has no effect on the initiation or course of labor and found no discoverable difference in the estrin content of the urine in normal and delayed labor.

Correlation of these findings to the onset of labor in the human has been attempted by clinicians in an effort to induce labor by the administration of estrin. Thus, Voron, Brochier, and Contamin successfully induced labor in prolonged pregnancy by the combined use of folliculin and posterior pituitary substance. Of course, one cannot accept this as estrin-induced labor because of the supplementary use of posterior pituitary substance. Gonnet, Banssillon, and Bucher successfully induced labor by means of estrogenic substance in addition to purging, quinine, and pituitary extract. One hesitates to accept this as an example of the successful induction of labor by estrogenic substance inasmuch as the latter three agents might in themselves be successful in inducing labor. Witherspoon, believing that the ascendancy of follicular hormone over the luteinizing hormone to be the cause of labor, attempted unsuccessfully to induce labor in 8 humans. Dodds and Robertson, in attempting to procure premature labor in 3 cases, using some 300 units of estrin, were successful in only one, but feel their results were inconclusive.

Perhaps one of the most definite clinical reports was the one by Robinson, Datnow, and Jeffcoate. They tried the effect of theelin in inducing abortion, premature labor, missed abortion, and in uterine inertia. Their attempts at inducing abortion were unsuccessful in 12 cases, although hemorrhage and uterine contractions were produced in 3. In 10 attempts to induce premature labor, quinine and pituitrin were used in addition to estrin, and labor resulted 5 times. The labors were noticeably shorter, which the authors attribute to the previously injected hormone. Success was obtained in 10 of 12 cases of missed abortion. In 7 of these 10, nothing but estrin was used. In the remainder, quinine and pituitrin were used in addition. They thought that estrin was of value in overcoming uterine inertia. The basis for the usage of estrin to terminate missed abortion was probably the report by Spielman, Goldberger, and Frank showing an absence of demonstrable blood estrin in such cases.

Savage, Wylie, and Douglass studied the effect of estrin administration to toxemic patients during pregnancy. They felt that in 4 cases the hormone possibly might have had some part in the induction of labor. They also believed that the short average duration of labor in the 9 patients treated with theelin might possibly have been the result of the theelin therapy. Reynolds (19, 20) is of the opinion that the increasing disproportion of the growth rates between the fetus and uterus toward the end of pregnancy is due largely if not entirely to the influence of estrin. This, in addition to the motility-stimulating action of estrin upon the myometrium, he feels, may be responsible for the onset of labor.

The accumulated data presented do not support the fact that estrin solely is responsible for the onset of labor, since additional factors were present which are equally significant. Nevertheless, the rôle of estrin has been

shown to be an important one, necessary in the onset of labor. Our attempts have been directed toward inducing labor in the human, near, at, or beyond, term by the administration of estrin without the aid of supplementary procedures or substances.

ANALYSIS OF PRESENT STUDIES

Estrin[1] was administered to 36 patients near, at, or beyond, term in an attempt to induce labor. Of these, there were 27 multiparæ and 9 primiparæ. Only those cases were chosen for this series in which there was no question of delivery by other than the vaginal route. The injections were given intramuscularly in the gluteal region and the total dosage per patient ranged from 10,000 to 350,000 international units. The number of injections to each patient varied from 1 to 6. Twenty-four patients received 1 injection, 9 patients received 2 injections, and 1 each received 3, 4, and 6 injections, respectively. When more than 1 injection was employed, the interval between injections was usually 24 hours. However, in 2 cases, the interval was 1 week, and in 1 case, the interval was 14 days.

The period of gestation ranged from 38 to 45 weeks. In 3 cases it was under 40 weeks, and in the 33 remaining cases 40 weeks or over. In 8 cases in which patients apparently responded following theelin administration, the period of gestation was 41 weeks in 5 and the 3 remaining were of 42, 44, and 45 weeks, respectively.

The membranes were intact in all 8 cases which apparently responded. This would rule out the possibility of at least one adjuvant contributing factor to the onset of labor.

We have been guided in the determination of whether estrin played a rôle in inducing labor by the experimental work of Parkes (14). He was of the opinion that the maximum effect of estrin on the uterus was exerted in from 36 to 48 hours after the last injection. We have chosen the onset of labor under 48 hours, following the last injection, as our basis for assuming that estrin might have been responsible for initiating labor in a particular case. Thus we feel that 8 of the 36 patients might have been successfully started in labor following estrin administration. In the 8 patients who responded, the time interval between the last injection and the onset of labor varied from 10 to 46 hours. Two of these 8 patients were primiparæ and 6 were multiparæ. In these 8 patients who apparently responded the dosage employed was 10,000 international units in 2 cases; 20,000 in 1; 30,000 in 1; 50,000 in 2; and 100,000 in the 2 remaining cases. From these figures, it is interesting to note that the apparent response was not directly related to the amount of estrin administered. It is for this reason that we did not attempt a further series with larger doses of this drug.

We arbitrarily assumed that 10 hours was a short labor for a primipara. In this series there were 4 primiparæ in whom labor was completed in less than 10 hours. The length of labor in the 5 remaining primiparæ varied from 14 to 45 hours. We first attempted to classify short multiparous labors, but in reviewing the previous labor records of these patients, it was noted that a number had short labors without using estrin. Therefore, to prevent inaccurate conclusions, we dispensed with those data.

There were no general or local reactions following the intragluteal injection of estrin though one case of pre-eclamptic toxemia might prove to be an exception. Her symptoms and blood pressure were under control but upon receiving 50,000 international units of estrin, her blood pressure began to rise within 24 hours, and finally reached 200/140 within 72 hours. This naturally precluded the further administration of estrin and prompted us to induce labor by rupture of the membranes.

This case history is comparable to one quoted in the series of Robinson, Datnow, and Jeffcoate. Their patient, however, developed an eclamptic seizure. The postpartum course in our series was unaffected, and there were no postpartum hemorrhages. There were no harmful effects upon the babies, and no deaths can be attributed to the procedure. The age of the patient, parity, and gravidity were not found to be factors in the response to estrin induced labors.

[1]Progynon B supplied through the courtesy of the Schering Corporation.

SUMMARY

It has been brought out that estrin can initiate and maintain uterine motility and contractility in animals and humans.

Experimental evidence has been cited to show that pregnancy in certain animals can be terminated by estrin administration.

We feel that the reports of successfully induced labor by estrin in the human are inconclusive. We are of this opinion because in practically all instances, estrin was employed along with other procedures or substances which might in themselves produce labor.

We have attempted to induce labor near, at, and beyond, term by administration of estrin without additional aid. Of 36 patients employed, it is possible that the onset of labor could have been attributed to the previously injected estrin in 8 cases. It is also possible that the estrin might have been responsible for the short labors in 4 of the 9 primiparæ in this series. The onset of labor bore no relationship to the dosage of estrin employed.

Thus, our findings merely suggest the possibility that labor in the human near, at, or beyond, term might be induced by estrin administration and that the duration of labor might be shortened by this method.

We wish to express our appreciation to Dr. William C. Meagher for permission to carry out these studies, and to Dr. S. R. M. Reynolds for his helpful criticism in the preparation of this report.

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PYELONEPHRITIC CONTRACTURE OF THE KIDNEY

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A CHRONIC pyelonephritis may heal or it may go on, to terminate in a pyonephrosis or in a contracture of the kidney (pyelonephritic contracture). The earlier authors, among them J. Aschoff and W. Israel, believed the latter condition to be very rare. But Braasch in 1922 showed that it not infrequently occurs as the outcome of renal infection and reported 28 cases of his own. In fact this condition has not received the attention in the literature which it justly deserves. Staemmler believes that it occurs more frequently than secondary contracture due to chronic glomerulonephritis. In 1,000 autopsies he found 55 cases of renal contracture, 27 of which were due to arteriosclerosis or arteriolosclerosis, 18 to pyelonephritis, and only 3 to chronic glomerulonephritis.

Haslinger has also demonstrated that there are various transitions of pyelonephritic contracture to hydronephrosis and pyonephrosis, which if more carefully studied would be seen to belong in this group.

In its purest form, pyelonephritic contracture consists of a fibrous shrinkage of the kidney as the result of a chronic suppuration. The resulting organ is small and its surface is granular. These changes are limited to the kidney substance proper. The pelvis itself is relatively free from pathological change.

To insure the development of this final pathological picture, certain conditions are necessary. The chronic suppurative process must necessarily be incited by an organism of low virulence. Since a pyelonephritis caused by such an organism will usually heal promptly if the renal pelvis drains properly, an obstruction to the outflow of the urine from the pelvis is usually necessary for the maintenance of the chronic suppuration. This obstruction must also be of low grade. For if the obstruction is of a higher degree, the changes of a hydronephrosis will precede and accompany those of the chronic suppuration and an infected hydronephrosis (large pyonephrosis) will result. If the infecting organism is one of high virulence, the suppurative process will not remain intratubular, but it will spread into the interstitial tissue, and form extensive abscesses and necroses in the renal substance. Coagulated plugs of fibrin and pus will plug the outlet from the renal pelvis and give rise to an empyema of the latter. The final picture will be that of a small pyonephrosis.

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PATHOLOGY

Most suppurative processes in the kidney arise as the result of a descending infection. Because of the large caliber of the renal capillaries, bacteria which are circulating in the renal blood stream have a tendency to be carried out through the renal veins to lodge subsequently in the finer capillaries of the liver, the lungs, the bone marrow, and the spleen. The normal kidney does not excrete bacteria.

Infections of the renal substance may, however, occur either spontaneously or because certain conditions exist in the kidney which favor the occurrence of such an infection. If the organisms reach the renal capillaries not in a finely separated state but in clumps, small mycotic emboli may form in the finer end-arteries which are situated mainly in the renal cortex. The resultant lesions are numerous cortical abscesses (nephritis aposthematosa). Such lesions, if not treated operatively (decapsulation), may go on to suppurative destruction of the kidney, which is accompanied by a clinical course with high fever. Operative removal of the kidney may then become necessary to prevent a threatening septicopyemia. In other, more favorable, cases the abscesses rupture after a period of days or weeks into the renal tubuli; and this occurrence is followed by intratubular suppuration and the development of a typical acute pyelonephritis which may then heal spontaneously.

In other cases, if an appreciable dissemination of virulent bacteria (especially cocci) occurs into the renal circulation, small necroses may develop in the capillary loops of the glomerular tuft, and through the resulting defects the bacteria may find their way mechanically into the glomerular lumina and thence into lumina of the renal tubuli. The organisms may then merely flow away with the urine (bacilluria), or an intratubular suppuration may follow (acute pyelonephritis). If renewed disseminations from a distant focus do not occur, the process has a tendency to heal spontaneously.

If an obstruction to the outflow of the urine from the renal pelvis exists, the kidney becomes susceptible to infection. The stagnation of urine in the pelvis and the resultant stretching of the pelvic wall produce a reflex slowing of the circulation through the kidney. This gives circulating bacteria a greater opportunity to lodge in the kidney. Further, bacteria which have found their way into the tubuli and which ordinarily would be washed away with the urine, now find an opportunity to remain in the stagnant urine, there to multiply and to produce infection. After an infection has occurred and intratubular suppuration has developed, the back pressure and lack of proper drainage serves to favor the maintenance of the process and to prevent healing. The intratubular suppuration may then continue for a period of months or even years. It is mainly with this latter type of chronic suppuration that we are concerned in cases of pyelonephritic contracture of the kidney.

In the early stages of chronic pyelonephritis the renal tubuli are seen to be packed with polymorphonuclear leucocytes. Then degenerative changes begin to appear in the tubular epithelum (Fig. 7). At first there is an albuminous degeneration, which may progress through the various stages of vacuolization, hyalin droplet degeneration, and finally to a necrosis and desquamation of the disintegrated epithelial cells into the lumen of the tubule. These changes may occur along the entire extent of the tubular apparatus, but they are usually most marked in the chief piece epithelium (proximal convoluted tubules). This involvement occasionally also extends to the delicate epithelial membrane covering the glomerular tuft and manifests itself as a swelling of the nuclei of the tuft. These swollen nuclei are then identified as belonging to epithelial rather than to endothelial cells (of the glomerular capillaries) by the fact that the capillaries of the tuft are well filled with blood. The changes described, occurring as a result of prolonged intratubular suppuration, may finally lead to a complete destruction and subsequent disappearance of the affected tubule (Figs. 9 and 10).

As the suppurative process in the lumen of the tubule progresses it eventually leads to secondary inflammatory changes in the interstitial tissue. At first a narrow zone of polymorphonuclear leucocytes appears around the periphery of the tubuli, especially in the medulla (Fig. 7). Then scattered zones of small round cell infiltration and plasma cells appear in the interstitial tissue, which spread and coalesce until finally the entire interstitial tissue is packed with a dense infiltration of round cells and plasma cells (Fig. 8). This inflammatory change eventually leads to a fibrosis of the interstitial tissue which subsequently shrinks (Fig. 9). Hyalinization may also occasionally take place.

The arteries in these fibrosed areas show secondary pathological changes in the form of a massive thickening of their walls and a narrowing of the lumina mainly as a result of a thickening of the intima (Fig. 13).

During the early stages of the process of contracture the glomeruli remain more or less intact. But they eventually undergo hyalinization, partly as a result of inactivity atrophy after their corresponding tubuli have disappeared and partly as a result of the ischemia caused by the secondary vascular changes described. This hyalinization progresses in a characteristic manner and begins in the parietal leaf of Bowman's capsule. A thin layer of hyalin appears under the epithelium, gradually thickens, and then spreads into the glomerular tuft at the hilus. Finally, the entire glomerulus is converted into a hyalin sphere (Figs. 10, 11, 12, and 13).

As the contracture of the renal tissue progresses, the interstitial inflammatory changes

gradually subside (Fig. 9). It is at this time that localized groups of lymphoid cells appear in the interstitial tissue which on closer examination prove to be well developed lymph follicles with well defined germinal centers (Fig. 14). In the normal kidney this lymphatic tissue appears in a rudimentary form as a delicate reticular stroma, which lies in the fibrous sheaths of the blood vessels and which is not demonstrable with the ordinary staining methods. But under the stimulus of a chronic suppuration in the kidney this lymphatic tissue proliferates to form well developed lymphatic follicles. Once they have appeared, these follicles persist; and they may remain long after all traces of the inciting suppurative process have disappeared.

The intratubular suppuration may persist until the very end or it may also gradually subside. The polymorphonuclear leucocytes then gradually disappear from the lumina of the tubuli. With the disappearance of numerous renal tubuli, compensatory changes occur in those remaining. The latter become dilated; their epithelium becomes flattened. Occasionally finger-like projections of epithelial cells sprout into the lumen. The dilated tubuli not infrequently contain coagulated colloid (Fig. 13).

The intratubular suppurative process sometimes causes a destruction of isolated segments of the tubule and the intervening portions remain temporarily intact. The proliferating interstitial fibrous tissue then spreads in to close the gap. At this stage the remaining tubular segment is seen in serial sections to terminate blindly at its proximal and distal aspects. Retention cysts form not infrequently in this manner. They are commonly seen in the form of obvious tubular segments which are dilated, in which the epithelium is flattened, and in which the lumen is filled with coagulated colloid. Occasionally they may grow to the size of a pinhead, a match head, a pea, a cherry, or even larger (Fig. 3).

GROSS PATHOLOGY

The shrinkage of the renal tissue may cause a varying reduction in the size of the organ. The kidney on the one hand may be of almost normal size (Fig. 3) and on the other may be 8 centimeters or even less in length (Fig. 4). The capsula propria is usually whitish, opaque, and thickened, and somewhat adherent in spots to the underlying renal substance, from which it strips leaving a somewhat smooth, finely granular, or a roughly granular surface (Fig. 1). The renal tissue itself is very firm and inelastic; and its cut surface reveals a pale yellowish, glassy hue. The cortical and medullary markings are largely obliterated (Fig. 2). The width of the cortex is greatly reduced and varies over different parts of the organ. The medullary pyramids are usually very pale and sometimes show a whitish radial striation (fibrosis). The papillæ may be greatly reduced in size. Their surface is, however, usually smooth.

Fig. 1. Pyelonephritic contracture. The surface of the kidney is roughly granular with large, uneven depressions and furrows. The capsula propria which is reflected to the left is thickened, opaque and white.

The renal pelvis may be of normal size or slightly dilated. The mucosa is usually normal in appearance. Occasionally its surface is wrinkled (Fig. 4). This is due to the fact that the shrinkage involves only the kidney substance proper and the pelvis subsequently accommodates itself to the latter.

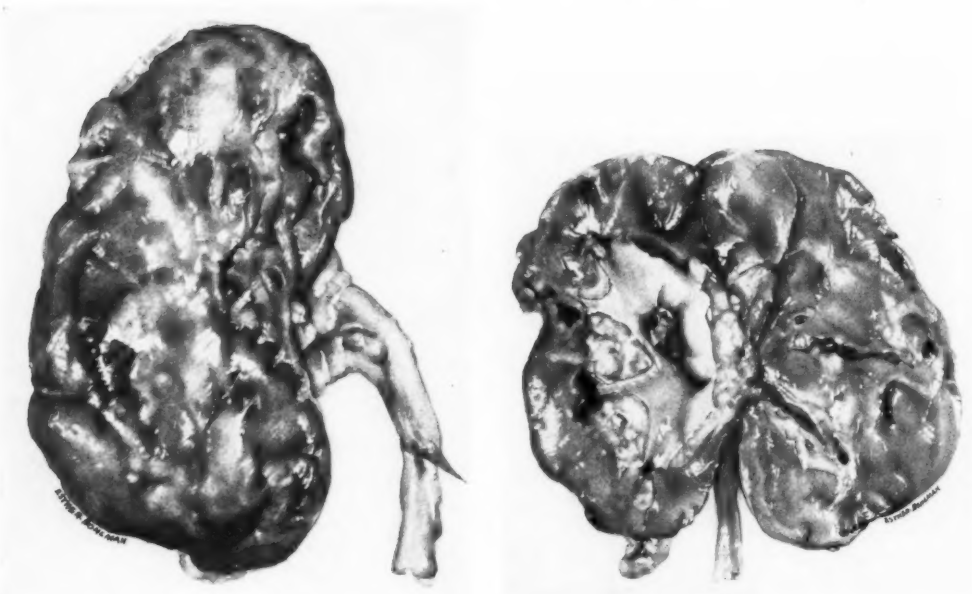

Fig. 2. Pyelonephritic contracture due to renal stone. a, left. Outer surface. The kidney is greatly shrunken and its surface is roughly granular. b, Cut surface. The cut surface has a pale, yellowish, glassy appearance and is very firm in consistency. Cortical and medullary markings are obliterated. There is a proliferation of the peripelvic fat. The renal pelvis contains a small calculus.

Staemmler and Dopheide have described pathological changes on the renal papillæ, and in the calyces, in the form of an epithelial proliferation and thickening. *But these, in our opinion, are not a part of the picture of pure pyelonephritic contracture, in which the surface of the papilla and the lining of the calycal wall are perfectly smooth and unaltered.* The changes, which the authors mentioned describe, belong rather to those cases in which a transition to hydronephrosis or to pyonephrosis is developing. Thus in the presence of an associated beginning hydronephrosis the papilla may be slightly flattened and widened, or cupped out. If a pyonephrosis is developing, the surface of the papilla may reveal a fungus-like proliferation, which on microscopic examination is seen to consist of necrotic tissue, which is fairly packed with bacteria—Bakterienrasen-(Necker)—and which is the result of an infection by virulent organisms. In still other cases the surfaces of the papillæ and the lining of the calyces have been converted into a thick, grayish to grayish-yellow, velvety coating. On microscopic examination this is seen to be due to a swelling and puffing up of the epithelial cells (foam-cell membrane). Occasionally the surfaces of the papillæ and the lining of the calyces may assume a silvery, glistening appearance due to a metaplasia of the lining epithelium which has been converted to a cornified epithelium. This is seen especially in those cases in which calculi are present in the pelvis.

A varying degree of perirenal and peripelvic fibrolipomatosis is usually present. The peripelvic fat spreads in from the hilus to fill the space defect caused by the shrinking of the renal substance.

In addition one frequently finds evidence of a low grade obstruction to the outflow of the urine from the renal pelvis. This may appear in the form of an aberrant vessel to the lower pole, a congenital valve at the ureter-

pelvic juncture, an anomalous insertion of the upper end of the ureter, or the presence of a pelvic calculus. It is also interesting to note the frequency with which fetal lobulation is demonstrable in cases of pyelonephritic contracture.

DIFFERENTIAL DIAGNOSIS

Pathologic differential diagnosis. Pyelonephritic contracture is most frequently confused with renal hypoplasia. Other conditions in which shrinkage of the renal substance occurs may also resemble the contracted pyelonephritic kidney grossly.

Renal hypoplasia. In this condition the kidney is usually very small as a result of incomplete development. This may manifest itself in a deficient development or absence of that portion of the renal anlage which comes from the nephrotom. The resulting kidney then shows a great sparsity or even a complete absence of glomeruli. In other cases the component parts of each nephron[1] are completely developed, but there is a decreased number of renculi,[2] so that instead of 12 to 18 of the latter there may be only 2 or 3 (Fig. 6). In renal hypoplasia the renal pelvis and ureter, as well as the renal blood vessels are usually small. Fetal lobulation is common.

But in spite of these differential points confusion may easily occur because infection and chronic suppuration are frequently present in hypoplastic kidneys. Further, kidneys which are not frankly hypoplastic but present congenital anomalies in the form of ectopy or of a pelvic malformation, are especially susceptible to infection and subsequent pyelonephritic contracture because of inadequate drainage of the renal pelvis. If, in addition, fetal lobulations persist, as often happens in such cases, one might very easily be misled into misinterpreting the resulting lesion as a renal hypoplasia.

In the later stages of pyelonephritic contracture, the suppurative process which has caused the damage may gradually burn out and disappear, leaving no trace of its previous existence in the renal tissue (Case 2). The resulting kidney will be small, and its surface will be granular. Superficial gross and microscopic study will apparently reveal a renal hypoplasia. The tubuli will be free of polymorphonuclear leucocytes; and round and plasma cell infiltration will be absent from the interstitial tissue. But on more careful study the following facts will become evident. Although the kidney is small, there are a normal number of renal papillæ. The renal pelvis is of normal size or larger, and merely seems smaller because its walls have become puckered in adjusting themselves to the shrinking renal substance. On microscopic examination the cortex is seen to be fairly packed with glomeruli in various stages of hyalinization (Fig. 13). Careful study of the interstitial tissue will reveal occasional hyperplastic lymph follicles which bear mute evidence to the previous existence of a severe suppurative process in the kidney as illustrated in Figure 14.

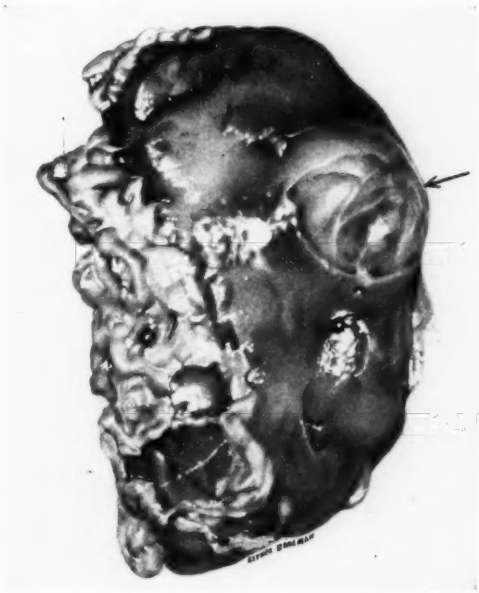

Fig. 3. Pyelonephritic contracture. In this case the kidney is almost of normal size. The surface is smooth. The renal tissue is, however, very hard and inelastic. In the upper pole a large cyst is seen (indicated by arrow).

[1] The nephron is the complete individual secreting element, consisting of a glomerulus with its corresponding tubular system.

[2] The renculus consists of a renal papilla with its corresponding medullary pyramid and cortex.

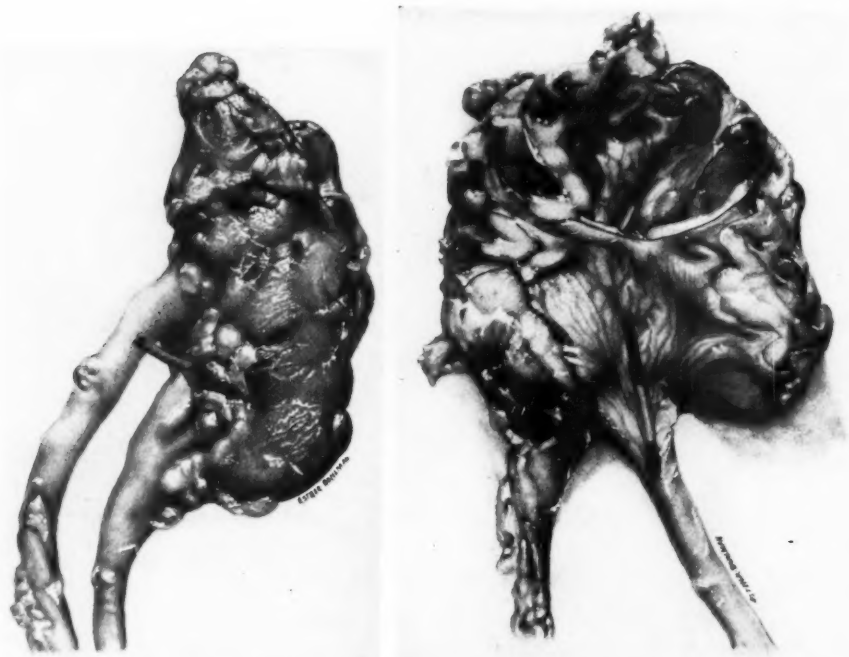

Fig. 4. Pyelonephritic contracture in a double kidney. a, left. Outer surface. The kidney is very small. The surface is granular. b, Cut surface. There is a ureteral catheter in each ureter and pelvis. The renal substance is very narrow. Cortical and medullary markings are obliterated. Both renal pelves are greatly wrinkled, because they have had to accommodate themselves to the shrinking renal tissue.

Pyelonephritic contracture is most commonly confused with renal hypoplasia because both of these conditions are usually unilateral. But if the former is bilateral, as may sometimes occur, the occasion may arise at autopsy when a differentiation between this lesion and other bilateral forms of renal contracture, notably renal arteriosclerosis (benign nephrosclerosis) and secondary contracture due to chronic glomerulonephritis, may become necessary. Grossly the kidneys may resemble one another in these three conditions. But since the intratubular suppuration persists in the great majority of cases of pyelonephritic contracture, a casual glance through the microscope will usually immediately identify the lesion. It is only in those somewhat uncommon cases in which the underlying suppurative process has run its course and burned out months or years previously that confusion may arise. It may then be very difficult, indeed, to make a differential diagnosis.

Renal arteriosclerosis. This condition is always bilateral although the degree of involvement may vary on both sides. Hyalinization of glomeruli, secondary interstitial inflammatory change, and a disappearance of tubuli may occur here too and give rise to some confusion. But careful study will readily show sclerotic changes in the arterial blood vessels as the significant and underlying lesion. Further the hyalinization will seem to spread into the glomerular tuft from the hilus; and it will not seem to begin in the peripheral leaf of Bowman's capsule as in pyelonephritic contracture. And here, too, the presence or absence of hyperplastic lymph follicles will tell us whether a severe suppurative process has preceded or not.

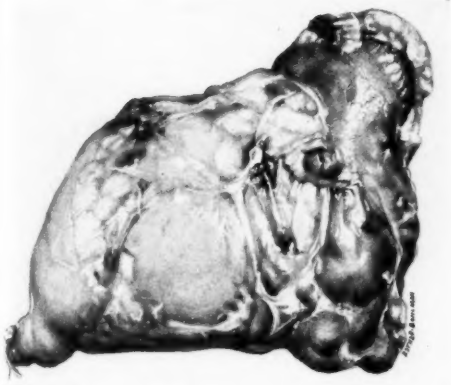

Fig. 5. Infected hydronephrosis with pyelonephritic contracture.

Secondary contracture due to chronic glomerulonephritis. Here the demonstration of adhesions of the glomerular tuft to the peripheral leaf of Bowman's capsule and the presence of half moon forms on the latter will usually bear testimony to the previous existence of inflammatory changes in the glomeruli. But in the advanced stages of contracture the differentiation may be exceedingly difficult; and only the presence or absence of hyperplastic lymph follicles will tell us which condition we are dealing with.

Finally, it must not be forgotten that mixed forms may occur, in that chronic suppuration and subsequent contracture may develop in a kidney in which other pathological changes are already present. Thus, for example, an old man with renal arteriosclerosis may, as the result of a bladder neck obstruction, due to a prostatic hypertrophy, develop a chronic bilateral pyelonephritis, which may lead to further contracture of the kidneys.

SYMPTOMS

The patient may complain of a dull ache in the renal region or subjective symptoms may be absent. Pyuria is usually present; but in the later stages of the disease the urine may be perfectly clear. Not uncommonly the contracted pyelonephritic kidney is symptomatically silent, and it may then appear as a chance finding at the autopsy table.

Fig. 6. Renal hypoplasia. The kidney measures 2 centimeters in length. There are only three renal papillæ all of which are imperfectly formed. The renal pelvis is small. Autopsy specimen.

Occasionally pyelonephritic contracture is bilateral. The general symptoms of total renal insufficiency then make their appearance. The urine is of low specific gravity and increased in quantity; and it may contain occasional hyalin or granular casts. Albumin may be sparingly present or absent. The blood pressure is usually elevated; and blood chemistry studies reveal a retention of nitrogenous products. The final clinical picture is that of a uremia in bilateral cases.

The recent clinical studies of Barker and Walters, Leadbetter and Burkland, Boyd and Lewis, and of others, inspired by the experimental investigations of Goldblatt and his coworkers, have shown that unilateral pyelonephritic contracture may cause a hypertension which is cured by nephrectomy.

DIAGNOSIS

The most important diagnostic finding is that of a marked functional defect in the involved kidney. The separated urine from this organ may contain pus cells and bacteria, but in the later stages of the condition it may be perfectly clear. It is, however, very pale and

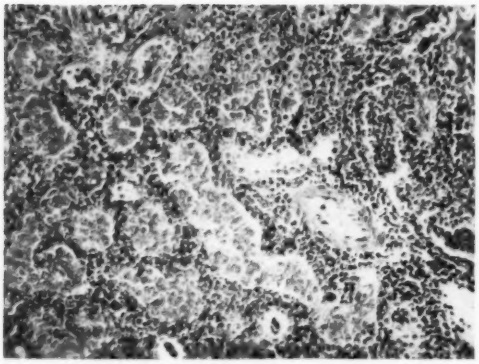

Fig. 7. Beginning pyelonephritic contracture. High power photomicrograph showing severe degenerative changes in the epithelium of the renal tubuli, and surrounding zones of polymorphonuclear leucocytic infiltration.

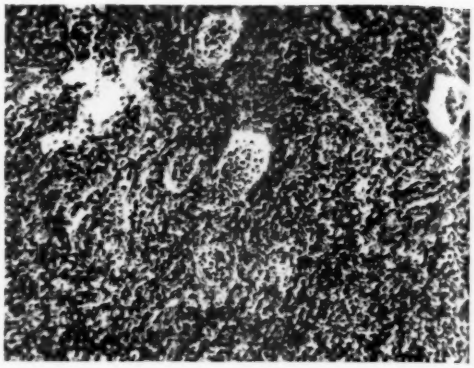

Fig. 8. High power photomicrograph showing extensive round and plasma cell infiltration of the interstitial tissue.

of low specific gravity. These findings may coincide exactly with those of renal hypoplasia. Pyelography, however, makes a differential diagnosis possible. In pyelonephritic contracture the renal pelvis is of normal size and form, or it may be somewhat dilated. In renal hypoplasia the kidney pelvis is smaller than normal and imperfectly developed.

In those cases in which the pyelonephritic contracture is bilateral the symptoms may coincide exactly with those of chronic glomerulonephritis with contracture, except that pyuria is usually present in the former. But, if the suppurative process has run its course and burned out, the urine may be clear. It may then be impossible to make a differential diagnosis antemortem. *In fact the possibility of a bilateral pyelonephritic contracture is rarely suspected in such instances, and a diagnosis of chronic glomerulonephritis with contracture is practically always made. Even at autopsy the error may persist unless a very careful microscopic study is subsequently carried out.*

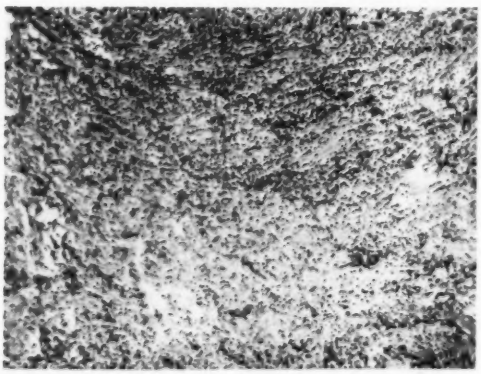

Fig. 9. Low power photomicrograph showing fibrosis of the interstitial tissue. The cellular infiltration is already subsiding.

SPECIMEN CASES

Case 1. Patient complained of left lumbar pain of 2 months' standing and frequency of urination of 6 months' standing. Physical examination revealed a somewhat undernourished white female of about 30 years of age. Neither kidney was palpable, but there was definite tenderness in the left costovertebral angle.

Urinalysis revealed, color, turbid; specific gravity, 1020; albumin, trace; sugar, negative. Microscopic examination showed urine to be loaded with pus cells. Gram stain revealed many gram negative, intracellular diplococci, morphologically resembling Gonococci.

Cystoscopic examination showed that the bladder capacity was normal, the right ureter orifice appeared to be normal, the left orifice was edematous and a tooth paste-like ribbon of pus exuded. From right kidney indigocarmin, intensive blue, appeared in 7 minutes; no pathological elements were noted. Left ureter could not be catheterized; no color was seen in 15 minutes.

Diagnosis: Left gonorrheal pyonephrosis. Left nephrectomy was done and postoperative course was uneventful.

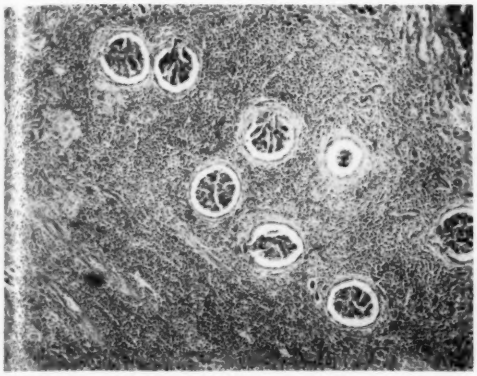

Fig. 10. Low power photomicrograph showing hyalinization of parietal leaf of Bowman's capsule of the glomeruli. The tubuli have largely disappeared from the interstitial tissue which is the seat of a small round cell infiltration.

Pathology. The left kidney measured 5 by 3 by 2½ centimeters. The capsule, which was somewhat thickened, whitish, and opaque stripped readily, leaving a roughly granular, pale surface upon which fetal lobulations were still evident. The kidney was very firm and inelastic in consistency. The cut surface was pale and had a somewhat glassy hue. The cortex was greatly narrowed and granular in appearance. Several pin-point sized whitish spots were seen in the cortex at the upper pole (pyelonephritic abscesses). The papillæ were flattened. The pelvic lumen contained a thick, greenish yellow pus. The pelvic mucosa was wrinkled; and numerous pinhead-sized, opaque nodules bulged from its surface (granular pyelitis).

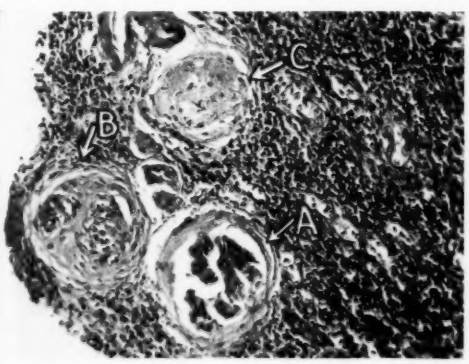

Fig. 12. The above illustration is a high power photomicrograph showing three stages in the hyalinization of the glomerulus. At *A* the hyalinization is seen confined to the parietal leaf of Bowman's capsule which is greatly thickened. At *B* the hyalin is spreading into the tuft. Finally, at *C* the glomerulus has been converted into a hyalin sphere.

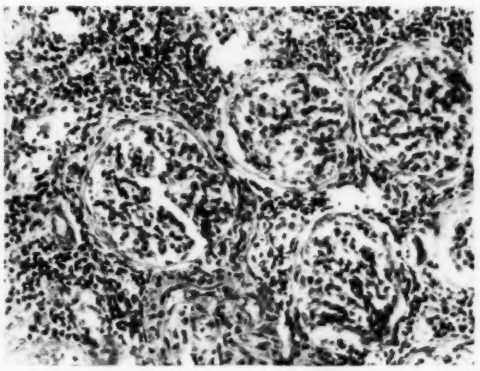

Fig. 11. High power photomicrograph showing hyalinization of parietal leaf of Bowman's capsule.

Microscopic examination revealed most of the glomeruli in various stages of hyalinization. There was considerable round cell infiltration in the interstitial tissue and numerous hypertrophic lymph follicles with well defined germinal centers were evident.

However, the tubuli seemed to be decreased in number. Most of the remaining tubuli were filled with polymorphonuclear leucocytes and amorphous débris. The epithelial cells revealed a severe albuminous degeneration. A few of the tubuli were dilated, their epithelial cells were flattened, and their lumina were filled with coagulated colloid.

Pathologic diagnosis: pyelonephritic contracture of the kidney.

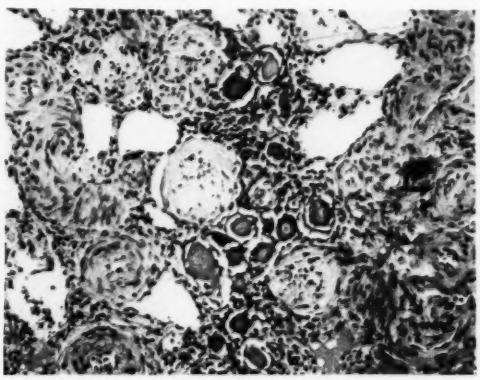

Fig. 13. High power photomicrograph showing the end stage of pyelonephritic contracture. All traces of intratubular suppuration as well as most of the interstitial inflammatory change have disappeared. The glomeruli have been converted into hyalin spheres. The few remaining tubuli are filled with coagulated colloid. The arterial blood vessels are greatly thickened (indicated by arrows).

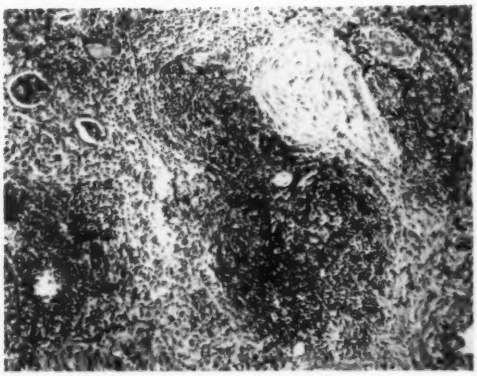

Fig. 14. Low power photomicrograph showing a hyperplastic lymph follicle with a well defined germinal center.

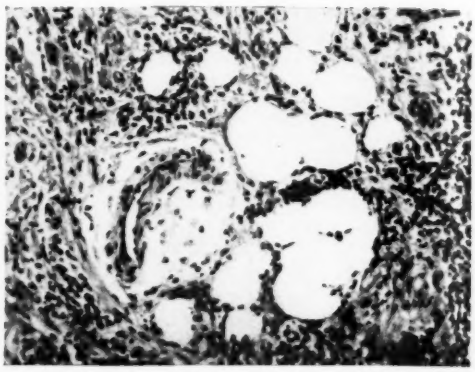

Fig. 15. High power photomicrograph showing hyperplastic fat tissue adjacent to a renal blood vessel in a case of pyelonephritic contracture.

CASE 2. On first admission patient complained of sticking pains in the left loin of 4 months' duration, and frequency of urination. Physical examination revealed a 30 year old female with slight tenderness in the left costovertebral angle. Neither kidney was palpable nor tender.

Cystoscopic examination revealed normal bladder capacity. The mucosa was dull red. The right ureteral orifice was inflamed. The left orifice was gaping and drawn up. Catheters were passed on both sides. From the right indigo appeared in 3 minutes; was intensive blue in 5 minutes. No pathological elements were noted. From the left indigo appeared in 5 minutes; blue not intensive in 7 minutes; 60 to 70 pus cells and Bacillus coli were found. Cystoscopic examination repeated 1 week later showed from right indigo intensive blue in 5 minutes. No pathologic elements noted. From left indigo blue, but not intensive in 5 minutes; 20 pus cells and bacillus coli noted. During the 7 months following the urine had progressively become less purulent but the left lumbar pain had persisted.

Cystoscopic examination revealed a normal bladder capacity. The trigone was reddened. The right ureteral orifice was normal. The left orifice was gaping. The right ureter was catheterized. On the left the catheter stopped at 1 centimeter. From the right side indigo, intensive blue appeared in 5 minutes. No pathologic elements were noted. From left no action, no color in 20 minutes. The bladder urine contained Bacillus coli and only an occasional pus cell.

Pyelography revealed a left renal pelvis of normal size. There was a slight clubbing of the terminal irregularities.

Left nephrectomy was performed.

Pathology. The kidney measured 7½ by 4½ by 3 centimeters. The capsule, which was somewhat thickened, white, and opaque stripped readily, leaving a granular surface. The cut surface revealed an obliteration of the cortical and medullary markings. The renal substance varied in thickness from ½ to 1½ centimeters. The pelvic lumen contained no pus and the pelvic mucosa was apparently normal except for a wrinkling of its surface.

Microscopic examination revealed the glomeruli somewhat closely grouped. A few were completely hyalinized, but most of them were intact except for a thickening and a hyalinization of the parietal leaf of Bowman's capsule. In many cases the nuclei of the tuft appeared swollen (these were probably of epithelial cells because the capillary loops were well filled with blood). The renal tubuli seemed to have decreased greatly in number, especially in the medulla. The chief pieces of the remaining tubuli revealed an extensive albuminous and hyalin-droplet degeneration. Some of these tubuli were dilated and their lumina were filled with coagulated colloid.

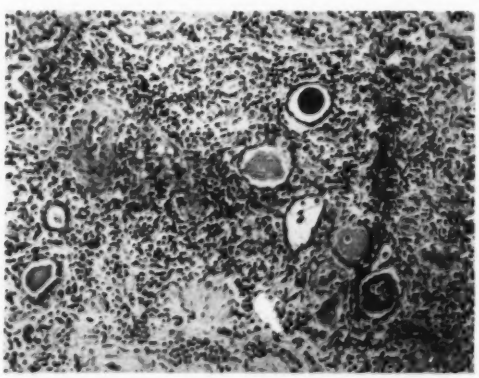

Fig. 16. Renal hypoplasia. The tubuli are dilated and filled with coagulated colloid. There is a complete absence of glomeruli. High power photomicrograph.

There was an extensive round cell infiltration of the interstitial tissue.

Pathologic diagnosis: pyelonephritic contracture. The kidney undoubtedly underwent a shrinkage between the first and last examinations. During this period the infection was gradually subsiding.

CASE 3. Patient complained of frequency of 6 months' duration and pyuria. Physical examination revealed a moderately well developed male of about 26 years. Neither kidney was palpable or tender.

Urine examination revealed color, cloudy; specific gravity, 1020; albumen, trace; sugar, negative. Microscopic examination showed that the urine was loaded with pus cells. Gram stain disclosed Bacillus coli.

Cystoscopic examination showed a normal bladder capacity. The mucous membrane was reddened. The left ureter orifice was normal. In the region of the right ureter orifice a large diverticular orifice was visible. The ureteral orifice itself could not be seen and apparently opened into the diverticulum. A ureteral catheter was passed on the left. The right orifice could not be catheterized. From the right no color was seen in 15 minutes. From the left indigo, intensive blue appeared in 5 minutes. No pathological elements were noted.

A cystogram revealed a walnut sized diverticulum on the right side of the bladder.

An intravenous urogram revealed normal concentration and normal contours of the left renal pelvis. The appearance of the dye was delayed on the right. The renal pelvis and ureter were greatly dilated.

Diagnosis: diverticulum of the urinary bladder; infected hydronephrosis right. A right nephrectomy was done.

Pathology. The kidney proper measured 6 by 3 by 3 centimeters. The capsule was thickened, gray and opaque and stripped with some difficulty leaving a coarsely granular surface. On the cut surface the kidney substance was seen to be less than ½ centimeter in thickness. It was somewhat pale and glassy in appearance and rather firm in consistency. The pelvis was enormously dilated and contained about 120 cubic centimeters of slightly purulent fluid. The calyces were widened and shortened. The papillæ were flattened and cupped out.

Microscopic examination revealed the glomeruli closely grouped and in various stages of hyalinization. The interstitial tissue especially in the cortex contained very few tubuli and was the seat of an extensive round cell infiltration. The remaining tubuli were dilated. This dilatation was more marked in the medulla. Most of the tubuli contained numerous polymorphonuclear leucocytes. A few tubuli were, however, filled with coagulated colloid. In the interstitial tissue numerous well developed lymph follicles with well defined germinal centers were to be seen.

Pathologic diagnosis: Infected hydronephrosis with pyelonephritic contracture.

CASE 4. Patient had suffered with left lumbar pain for 1 year. Physical examination revealed a well developed male of about 35 years of age, apparently not acutely ill.

Cystoscopic examination revealed the urine cloudy; the bladder mucosa and the ureteral orifices revealed no abnormalities; catheters were passed on both sides. From right the indigo appeared, intensive blue, in 7 minutes. No pathological elements were noted. From the left the indigo was light blue in 15 minutes. Many pus cells and red blood cells were noted.

X-ray examination: The flat plate revealed a staghorn calculus in the region of the left renal pelvis. Pyelography revealed a slight dilatation of the renal pelvis and of the calyces.

A left intracapsular nephrectomy was done.

Pathology. The kidney was of normal size. The surface was finely granular and glistening. On the cut surface the parenchymal markings were well seen. The renal substance, however, had a yellowish, glossy hue and was very hard on palpation. A large staghorn calculus filled the renal pelvis.

Microscopic examination showed considerable albuminous and some hyalin-droplet degeneration of the chief piece epithelium. The tubuli seemed to have decreased in number and there was considerable fibrosis and hyalinization of the interstitial tissue, especially in the medulla. A few of the tubuli contained scattered groups of polymorphonuclear leucocytes. Numerous areas of rather dense round cell infiltration appear in the interstitial tissue. Well defined follicles of lymphoid tissue with well defined germinal centers were also seen. Some of the glomeruli showed a beginning hyalinization. The hyalin appeared in a thin layer under the epithelium of the parietal leaf of Bowman's capsule and in small clumps in the tufts.

Pathological diagnosis: staghorn calculus with beginning pyelonephritic contracture of the kidney. This represents a pyelonephritic kidney in the stage of beginning contracture. The ascending intratubular infection has already largely burned out. The interstitial inflammatory change now commands the field. The tubuli have begun to disappear and hyalinization of the glomeruli with interstitial hyalinization is beginning.

CASE 5. Patient had been hospitalized for a tubuculous hip. During this time pus cells and bacteria (Bacillus proteus) were found in the urine. Subsequently (during the past 3 weeks) she developed severe sticking pains in the right lumbar region. Physical examination revealed a well developed female of about 25 years of age.

Cystoscopic examination revealed cloudy urine; bladder capacity, normal; the mucous membrane, slightly reddened. Catheters were passed on both sides. From right indigo carmin, light blue, appeared in 8 minutes. 6 to 8 leucocytes were noted as well as the Bacillus proteus. From left, indigo, intensive, appeared in 4 minutes. No pathological elements were noted.

Nephrectomy was performed.

Pathology. The kidney was of normal size. The capsule stripped readily leaving a smooth surface of pale yellowish hue. The cut surface had a slightly glassy hue. There was an obliteration of the cortical and medullary markings, and the renal substance was hard and inelastic in consistency. The pelvis and ureter revealed no abnormalities. Two small urate stones appeared, one in a lower calyx.

Microscopic examination disclosed very few tubuli. There was considerable interstitial round cell infiltration. In the few remaining tubuli the epithelial cells were necrotic and in many places desquamated into the lumen, in which a few polymorphonuclear leucocytes could still be seen. Most of the glomeruli revealed a swelling of the nuclei of the tuft and a poor filling of the capillary loops. In many there was a beginning hyalinization of the parietal leaf of Bowman's capsule.

Pathologic diagnosis: renal stone with pyelonephritic contracture of the kidney.

CASE 6. Five months previous to admission the patient complained of abdominal cramps followed by jaundice. This subsequently cleared up and she was well for 2 months. Then there were several recurrences of the cramps which were always in the epigastric region. During this time she lost 30 pounds in weight. A complete medical examination was negative except for the finding of a few pus cells in the urine and a small calcific shadow in the region of the left kidney.

Cystoscopic examination showed the urine, cloudy; the bladder, essentially normal. Catheters were passed on both sides. From right indigo, intensive blue, appeared in 6 minutes. No pathological elements were noted. From left indigo, very pale blue, appeared in 15 minutes, many leucocytes were noted. X-ray examination revealed a calcific shadow the size of an almond in the region of the left renal pelvis. Pyelography revealed a slight dilation of the pelvis and of the calyces.

A left intracapsular nephrectomy was done.

Pathology. The kidney measured 8 by 4 by 3 centimeters. The surface was roughly granular and showed irregular humps. Where the capsule was stripped (at operation) the renal substance was adherent in places and tore. On the cut surface the kidney appeared slightly paler than normal and granular, and very firm on palpation. The cortex was very narrow (1 to 2 millimeters) and of irregular thickness. The pyramids were dark red with longitudinal whitish lines (fibrosis). The papillæ were smaller than normal but smooth. The pelvis was white and marbly but smooth, and contained a black rough stone the size of a shelled peanut. There was an increase in the peripelvic connective tissue, which was harder and more yellow than normal.

Microscopic examination disclosed that the glomeruli appeared closely packed and some of them showed a beginning hyalinization. The medullary tubules were dilated and there was considerable interstitial medullary fibrosis. There was also a marked round cell infiltration of the interstitial tissue from which many of the tubules seemed to have vanished. Some of the remaining tubules still contained groups of polymorphonuclear leucocytes.

Pathological diagnosis: renal stone with pyelonephritic contracture of the kidney.

SUMMARY

1. Pyelonephritic contracture consists of a shrinkage of the renal substance as a result of chronic suppuration.

2. The condition is rather common.

3. Various transitions to hydronephrosis and pyonephrosis are frequently seen.

4. Its development in a pure form depends upon the presence of a low grade suppuration and usually of a low grade obstruction. It is, therefore, not uncommonly seen in cases of pelvic calculus.

5. It is most frequently confused both clinically and pathologically with renal hypoplasia.

6. Pyelonephritic contracture is usually unilateral.

7. The most important diagnostic finding is that of a marked functional defect in the involved kidney. The pyelogram reveals a pelvis which is of normal size or slightly dilated.

8. Pyelonephritic contracture is occasionally bilateral. The symptoms may then resemble those of chronic glomerulonephritis with contracture.

9. Unilateral pyelonephritic contracture may cause a hypertension which may be relieved by nephrectomy.

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CARCINOMA OF THE BREAST

End-Results: Massachusetts General Hospital 1930, 1931, and 1932

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THE following paper is the seventh in a series of communications reporting the end-results of operation for carcinoma of the breast performed at the Massachusetts General Hospital, and covers cases treated during the 3 year period, 1930–1932 inclusive. Both private and ward patients are considered, and this report has been arranged, in so far as possible, in the same manner as the former reports in order that results may be compared with the previous findings.

Evaluation of therapy obviously must depend upon careful end-result studies, and in malignant disease a protracted period of observation is necessary before reliable conclusions can be reached. Likewise, accurate knowledge of the life history of the disease offers an invaluable control in appraising the results of treatment. The studies of Daland on untreated carcinoma of the breast are of inestimable value in contributing to our knowledge of carcinoma of the breast, as is also the recent report of Nathanson and Welch on life expectancy and incidence of the disease. Proper use of the curves presented by these authors may permit tentative appraisals of the results of a method of treatment before the arbitrary 5 year follow-up period has elapsed, as suggested by Meigs.

The first report in our series from the Massachusetts General Hospital (5), published in 1907, was based on a minimum 3 year follow-up period. Subsequent reports (3, 4, 6, 10, 11) have been based on a 5 year follow-up period. It is recognized that this is a purely arbitrary interval, and that a certain number of recurrences will take place after an apparent 5 year "cure." However, the attempt to follow cases for a longer period in a general hospital clinic is very difficult and the increase in untraced patients tends to vitiate data based on a longer follow-up period.

It will be observed that each series of cases we have studied has shown improvement in results when compared with previous series. If at any time we had instituted any new adjuvant to our method of treatment, the conclusion would be inevitable that the increased number of cures was due to the added factor. Two factors certainly have been effective in improving our results, namely, improved surgical technique and better selection of cases suitable for attempt at operative cure. The formation of a Tumor Clinic at the Hospital, and the assignment of cases of carcinoma of the breast for special study to members of the Tumor Clinic staff led to a standardization of operative technique in a radical operation (13). Intensive study, especially of results of

operation, led to a clarification and restriction of operability.

However, it is probable that a large part of the improvement shown in the results of surgical treatment in recent years has been due to a more careful selection of cases suitable for surgical intervention, and a greater reluctance to employ surgery in conditions in which experience has demonstrated that surgery is useless or prejudicial. Many patients have been saved an operation following routine x-ray studies of the chest and skeleton with the detection of metastatic foci in cases which might otherwise be assumed to be operable. The availability and effectiveness of radiation therapy as a palliative procedure in borderline and poor risk patients has also sharpened the criteria of operability.

It is impossible to determine how much of the improvement in the results of operation may be attributable to the campaign of cancer education carried out in the past 13 years by the American Society for the Control of Cancer, the American College of Surgeons, and the Massachusetts Department of Public Health. In spite of the narrowed criteria of operability, the operability of patients with carcinoma of the breast at the Massachusetts General Hospital remains at about 80 per cent of admissions. A considerable but undetermined number of patients are intercepted in the Out-Patient Department and treated for inoperable carcinoma without admission to the Hospital, and it is also probable that physicians refer patients to the hospital that seem to them to be favorable for cure; while their patients with advanced conditions are referred to some of the more recently established radiological institutions for palliative treatment; hence our 80 per cent operability.

OPERABILITY

Carcinoma of the breast is operable when the disease is confined to the breast, or to the breast and axilla. The primary tumor must be movable in relation to the chest wall, and must not present extensive skin involvement, skin metastases, or the subepidermal infiltration known as "inflammatory" carcinoma. The axillary nodes must be movable in relation to the chest wall and great vessels, and these nodes must be few in number. There must be no evidence of disease in the supraclavicular areas or in the opposite axilla, nor of metastatic disease in the lungs, pleura, liver, or skeleton. Patients in the last 2 series have had pre-operative x-ray studies to rule out the presence of skeletal and pulmonary metastases.

Comparison with results achieved in other clinics must be made with caution and reservation. In analyzing the cases, we have employed the abstract record sheets advocated by the American College of Surgeons and have adopted their classification. If these sheets were in general use, it would simplify the comparison of various methods of treatment of malignant disease. An attempt to broaden the field of operability may result in an occasional cure but only in a marked falling off in percentage of cures. On the other hand, rejection of cases with palpable axillary lymph nodes would result in a marked apparent improvement in percentage of cures by denying to a considerable group the possibility of surgical intervention.

As a matter of fact in certain clinics the hope has been entertained that by means of pre-operative x-ray therapy cases primarily inoperable, would be rendered operable, and that hence the benefit of radical surgery could be offered to more advanced lesions. Investigation of this possibility is a legitimate field for clinical study. We have not employed this procedure in any of the cases in this series. The improvement in our statistics cannot be due to the combined treatment by surgery and radiation, for pre-operative radiation was not employed in any case, and relatively few patients received postoperative prophylactic radiation. This fact is significant in comparing these results with those obtained by other observers who suggest that the improvement in their statistics is due to the employment of radiation therapy in conjunction with surgery. In recent years there has been a tendency in some clinics to carry out less than radical operations in certain selected cases. Since clinical appraisal of the extent of the disease, especially as regards axillary lymph node involvement, is highly fallible, we can entertain no sympathy for this practice.

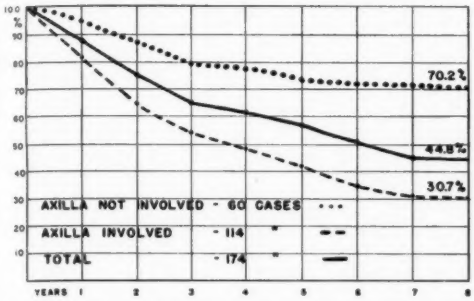

Chart 1. Percentage of cures at yearly intervals in carcinoma of breast on the basis of axillary involvement.

TABLE I.—185 PRIMARY OPERABLE CASES

	Cases	Cases
Disease limited to the breast	69	
Died without recurrence less than 5 years. Suitable for study	9	60
Disease limited to breast and axilla	116	
Died without recurrence less than 5 years. Suitable for study	2	114
Total cases for end-result study		174

ANALYSIS OF CASES

The group represents the cases seen in the General Hospital, the private wards, and the semi-private wards. Operation with the hope of cure was performed during this 3 year period on 185 patients divided as follows: General Hospital, 73; private wards, 43; semi-private wards, 69. The end-result is known in every case.

The Tumor Clinic was in charge of all the patients operated upon in the General Hospital and these patients were operated upon by members of the Tumor Clinic staff, and a large proportion of the patients in the private wards were operated upon by the same group of surgeons. Thus 134 of the operations were performed by members of the Tumor Clinic staff and 51 by 17 other surgeons, only 2 of whom performed more than 5 operations in the 3 year period studied.

In the analysis of the cases, we have followed the same rules adopted in the previous reports. Operative deaths are considered as failures. Patients dying with recurrence after 5 years or patients living from 5 to 8 years with recurrence are considered as "dead of disease." Untraced patients, of whom there are none in this series, are also considered as having died of recurrence. Patients dying of other causes, such as appendicitis, within 5 years from the date of operation are excluded as inconclusive.

The same type of operation was performed by all members of the Tumor Clinic staff and those performed by other surgeons varied only in unessential details. The radical operation consisted of the removal of the breast, both pectoral muscles and the contents of the axilla. A large amount of subcutaneous tissue extending from the sternum to the border of the latissimus dorsi was removed but enough skin was preserved to allow closure in most instances. That this procedure was justified is shown by the fact that in the 133 cases in which we have data there was a recurrence in the region of the wound in only 10 cases (7.6 per cent).

Of the 185 patients with carcinoma of the breast suitable for an attempt at cure by radical operation admitted to the hospital during the 3 year period, the disease was limited to the breast in 69 cases (37 per cent) and in 116 the axilla was involved. Eleven patients died of other disease within 5 years from the date of operation and have been excluded as inconclusive in studying the end-results.

Of the 174 cases available for end-result studies 78 or 44.8 per cent are living without evidence of disease from 5 to 8 years after operation. All cases have been followed for 5 years after operation and many of them for 6 to 8 years. Five years after operation 56.3 per cent are living. This figure is compared with those obtained in the previous groups studied: Percentage of cures, 1894–1904, 19; 1911–1914, 27; 1918–1920, 30; 1921–1923, 35; 1924–1926, 41; 1927–1929, 43; 1930–1932, 45. The percentage of cures in the cases in which the disease was limited to the breast was 70.2 but if the axillary lymph nodes were involved the percentage of cures was only 30.7. The figures obtained in the 1927–1929 group previously reported were 74.8 per cent and 24 per cent respectively. In general it may be said that if the disease is limited to the breast the chances of surgical cure are 3 out of 4, and if the axillary nodes are involved, 1 in 4.

TABLE II.—DURATION OF DISEASE—RESULTS

Pre-operative duration—months	No. patients living	No. patients died	Cures per cent
Less than 1	11	14	44
1 to 3	20	21	49
4 to 6	10	15	40
7 to 12	10	13	43
13 to 24	8	6	57
25 to 36	1	4	20

(Data on 133 cases)

The percentage of survivals at yearly intervals is shown graphically in Chart 1.

Operative mortality. There were 3 deaths attributable to the operation, an operative mortality of 1.6 per cent. One death was due to cardiac failure; one patient died as the result of sepsis, and 1 from pneumonia and dementia.

Duration of disease and results. In the present series there was slightly less delay from the time the tumor was first noticed to the time of operation than in the previous groups studied. The average pre-operative duration in the cases in which the disease was limited to the breast was 2.8 months, and in the cases in which the disease had extended to the axilla 5.3 months. The figures imply that patients are seeking advice for a suspicious tumor of the breast at an earlier date than formerly.

As previously stated, the duration of the disease before operation in a large series of cases apparently has little relation to the results of treatment, but it is important in the individual case (Table II). The prognosis has always been found to be worse when the disease is of short duration if the cases are studied as a group. This may be explained, in part at least, by the fact that the more malignant tumors are of rapid growth and attain a size which causes the patient to seek medical advice relatively quickly. The percentage of cases in which the disease was confined to the breast was less than in the last 2 groups studied. It was interesting to note that in the patients in the private wards the percentage of cases in which the disease was confined to the breast alone, as well as the number of cases of low malignancy, was greater than in the general hospital. The figures are not conclusive but suggest that the social status of the patient may have some relation to the disease. This possibility has been suggested by several authors.

TABLE III.—AXILLARY NODES

	Positive No.	Per cent	Negative No.	Per cent	Total cases
Palpable	53	87	8	13	61
Not palpable	42	53	37	21	79

Extent of disease—results. The extent of the disease, that is whether it is limited to the breast or whether it has extended to the axilla, is apparently the most important single factor influencing the result of operation. Although the pre-operative duration of the disease was less in this series than in previous series, the percentage of patients with positive axillary nodes was greater. The percentage of cases limited to the breast is as follows: 1894–1904, 33; 1911–1913, 31; 1918–1921, 30; 1921–1923, 28; 1924–1926, 41; 1927–1929, 38; 1930–1932, 37. In the patients in the private wards the disease was confined to the breast in 53.5 per cent while in the general hospital only 35.5 per cent were in this group. In the semi-private wards, where the patients represent an intermediate social group, the disease was limited to the breast in only 29 per cent of the cases.

Data as to the presence or absence of clinically palpable axillary nodes were available in 140 cases. In the 61 cases in which nodes were noted on physical examination positive evidence of cancer was found in 53 (87 per cent) on microscopic examination of the specimen. In the 79 cases in which no axillary lymph nodes could be felt, cancer was found on dissection of the axilla in 37 (46 per cent) (Table III).

Pathology. Since Broder's paper was published in 1923 on the grading of malignant tumors and the relation of the degree of malignancy to the prognosis we have graded all tumors, placing them in 3 groups instead of 4. The grade of malignancy has been found to have a definite bearing on the prognosis. It is more difficult to grade an adenomatous than a squamous cell tumor; and although there was some difference of opinion among pathologists, they agreed as to the grade in most instances. The criteria employed were: (1) the amount of differentiation of the cells, that is, the tendency to form glands and evidence of secretion; (2) the uniformity in size and shape of the nuclei; (3) the number of mitoses; and (4) the tendency of the cells to infiltrate.

That this grading is of distinct value in making a prognosis has been shown in the previous papers and is borne out in the analysis of this group. The grade of malignancy is second only to the extent of the disease in determining the prognosis in a given case. The majority of the cases fall in Group 2. There were relatively few cases of low malignancy (Group 1), but a larger percentage were in the group of high malignancy than was the case in the previous series.

There were 19 cases in the low malignancy group. One was an operative death and 3 patients died of other diseases within 5 years from the date of operation and are therefore inconclusive. Of the 15 remaining patients, 13 are living without disease and are classed as cures (86 per cent). The axillary nodes were involved in only one of the 19 cases. Fifteen cases were classed as grade 1; 14 of these patients (93.3 per cent) showed no extension of the disease to the axillary nodes.

Eighty-five cases were classed as grade 2 with 51 per cent cures. The disease was limited to the breast in 26 patients, or 30 per cent of the cases in this group. Seventy-one cases were classed as grade 3. There were 31 per cent cures and in 18 patients, or 25 per cent, the disease was confined to the breast.

The percentage of cases in the 3 grades of malignancy living at yearly intervals is shown graphically in Chart 2. In making this chart the 3 cases dying as the result of operation have been excluded. There were 5 cases of Paget's disease of the nipple. One patient died of other disease within 5 years, 2 died of recurrence, and 2 are well. There was also 1 case of squamous cell cancer in which the tumor was deeply situated in the breast. This patient died from metastases.

The tumors of high malignancy were more common in the younger age group, but tumors of low malignancy did occur and in these the prognosis was as favorable as tumors of the same degree of malignancy occurring in older patients. In other words, the prognosis depends on the degree of malignancy and not on the age of the patient as is often stated. The manner in which we classified 174 cases as to age and degree of malignancy is as follows: There were 29 cases in the age group

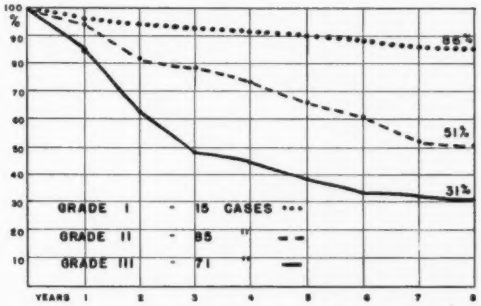

Chart 2. Percentage of cures at yearly intervals in carcinoma of breast on the basis of the pathological index of malignancy.

18 to 40 years, with grade 1, 3 per cent; grade 2, 42 per cent; grade 3, 55 per cent. There were 94 cases in the age group 41 to 60 years, with grade 1, 11 per cent; grade 2, 48 per cent; grade 3, 41 per cent. There were 51 cases in the age group 61 to 80 years, with grade 1, 8 per cent; grade 2, 60 per cent; grade 3, 32 per cent.

Age and results. The statement often made that the prognosis in cases of cancer of the breast is worse in women under 40 than in older women is suggested by the analysis of this series. There is, however, a great difference in the figures in the last 3 groups studied. In the 1926–1928 series cure was obtained in 34 per cent of the patients under 40 years of age. In the 1927–1929 series there were only 10 per cent of cures in the group, while in the present series there were 31 per cent cures. That tumors of high degree of malignancy are more common in women under 40, has been shown by one of us (12) and is borne out by our figures. This fact is the reason for the poor prognosis in young women. The point has been discussed previously under the heading, "Pathology and Results."

If the cases are placed in 3 age groups the percentage of cures is as follows: 31 per cent of 29 cases, 18 to 40 years; 48 per cent of 96 cases, 41 to 60 years; 50 per cent of 46 cases, 61 to 80 years. The youngest case in the group was 18 years of age, the oldest 78; 22.5 per cent were under 40 years of age.

Exploratory operation—biopsy. An exploratory operation and biopsy to verify the clin-

ical diagnosis was performed in 34 cases. In 18 of these patients the disease was limited to the breast while in 16 the axillary nodes were later found to contain cancer. Fifty-four per cent of these operations resulted in cure. The figures are not significant but suggest that metastases may occur early and before the primary tumor attains a size sufficient to present the characteristic clinical picture of cancer. The method of biopsy employed consisted of an incision directly into the tumor and removal of a small portion for examination. If the tumor was found to be cancer, the wound was packed with a sponge wet with 10 per cent formalin and closed. The instruments and gloves were then changed and immediate radical operation performed.

We have felt that the removal of a specimen for diagnosis unless followed immediately by radical operation was a dangerous procedure, and also that aspiration or punch biopsy should not be employed in operable cases on account of the possible danger of disseminating the disease.

Site of recurrence. Of the 93 patients dying of metastases the site of recurrence is known in 60 instances. There were multiple metastases in 21 cases. The most common site of recurrence was the lungs although bone metastases were nearly as frequent. The sites of recurrence were as follows: local, 10; regional nodes, 11; lung, 25; bone, 24; brain, 8; opposite breast, 6; and liver, 9. The striking point is the relatively few cases of local recurrence, 10 cases in 133 or 7.6 per cent, although sufficient skin was preserved at the time of operation to allow the wound to be closed. We believe this relatively low percentage of local recurrence is due to a careful selection of the cases and to the fact that a large amount of subcutaneous tissue was removed. The figures should be accepted with some reservation for we have such data on only 77 per cent of our cases. It is difficult to say in the 6 cases, in which the disease was later found in the other breast, whether this represented a metastasis or a new tumor. We have considered them as cases of recurrence. We agree with Scott that recurrence in the operative field is an indication of either a faulty selection of cases for operation or of improper surgical technique.

Twenty patients living 5 years after operation died later of recurrence. In 12 of these evidence of recurrence was present before the arbitrary 5 year period had elapsed but the 8 others were apparently well at that time and showed evidence of metastases later. We have estimated that about 15 per cent of patients living apparently free of disease at the end of 5 years will eventually die of recurrence.

SUMMARY AND CONCLUSIONS

This report is the seventh in a series of end-result studies of carcinoma of the breast treated at the Massachusetts General Hospital.

Five to 8 year cures were obtained in 70 per cent of cases in which disease was confined to the breast, in 31 per cent when the axillary nodes were involved, and in 45 per cent of the entire group.

The improvement in curability, as compared with previous series, may be attributed to standardization of the radical operation and to better selection of cases. Some improvement may be due to shortening of the preoperative duration of the disease as a result of educational programs. We are unable to attribute any of the improvement in results to radiation therapy which was not employed in this series.

Clinical appraisal of axillary lymph node involvement is highly fallible. Nodes may prove to be involved in nearly half of the cases in which no nodes can be felt clinically, and in half the cases in which exploration of the primary tumor in the breast is necessary to establish the diagnosis of carcinoma. Nearly two-thirds of the entire group proved to have axillary node involvement at the time of operation. There does not appear to be any tendency in recent years for this advanced operable group to diminish in relation to the total group.

The pathological index of malignancy is of great significance in prognosis. In high grade malignancy the tendency is to metastasize earlier and there is a markedly lessened chance of cure by radical operation.

The age of the patient is of prognostic importance only in so far as younger patients tend to present higher grades of malignancy and earlier metastasis to the axilla.

Exploratory incisions, followed by immediate radical operation, do not seem to jeopardize the likelihood of cure.

Recurrence in the operative field is rare if proper selection of cases and proper operation are carried out. Wide skin removal at operation, requiring skin grafting for closure, is not often necessary.

The authors wish to express their thanks to the staff of the hospital for permission to include certain cases.

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ONE-STAGE THYROIDECTOMY FOR THYROTOXICOSIS IN THE AGED

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IN the early days of the development of thyroid surgery postoperative crisis constituted the commonest cause of death and the greatest dread of the surgeon. Improvement in technique lowered the mortality, but on the whole it remained a formidable handicap. The introduction of preliminary ligation and of multiple stage operations seemed to lessen the number of crises and to reduce the mortality. What part these two steps actually played in reducing mortality, as compared with the general improvement in technique and the tendency of patients to gravitate toward surgeons and clinics particularly interested in thyroid surgery, must be a matter of conjecture. With the introduction of iodine as a means of preparing the thyrotoxic patient for operation, mortality and the incidence of postoperative crisis fell rapidly. By this time the proportion of patients subjected to preliminary ligation and multiple stage operations had reached fantastic proportions in some clinics. With the continued use of iodine the need for these various preliminary steps was recognized by many to be lessened, but that they are still necessary continues to be believed. Many authoritative writers accept the value of these procedures as established.

Marshall, of the Lahey clinic, writes, "In our hands the utilization of stage operations has been one of the most valuable means of preventing operative fatalities." In a recent paper Lahey (4) says, "If I were asked to state what is the most important single feature related to the surgery of hyperthyroidism, I believe I would say that it is the preoperative decision as to how severe the thyroid intoxication is and as to whether the patient will probably require multiple stage procedures." Twenty-two per cent of all patients operated upon in the Lahey clinic for all types of hyperthyroidism underwent multiple stage procedures (5). Seventy-five per cent of all patients 60 years of age or over with toxic goiter have been operated upon in stage operations in this same clinic (13). At the Crile clinic the divided operation is reserved for the "bad risk" cases. Between 1930 and 1935, 13 per cent of the total number of thyroidectomies were performed in stages and in only 6 per cent were ligations performed (2). At the Mayo clinic the percentage of multiple stage operations decreased from 70 per cent in 1921 to 1 per cent in 1926 (9). Pemberton, in 1929, wrote, "I am convinced that 98 per cent of all patients with exophthalmic goiter can be made safe surgical risks by proper medical management and that the stage operation as a supplemental preparatory measure is indicated in a very small group of patients. During 1927 operations were performed on 1,520 patients with exophthalmic goiter. In only 8, or 0.52 per cent, of these were there indications for dividing the resection into two stages. Eleven patients died, a mortality of 0.72 per cent. Two died following the first stage lobectomy."

We believe our experience justifies a critical re-opening of the question of multiple procedures in thyroid surgery for thyrotoxicosis. It is not enough for the proponents of these measures to establish that the mortality of thyroidectomy in thyrotoxicosis has fallen year by year. Improved technique and specialization have reduced the mortality in practically all departments of surgery. The attitude, so commonly held, that after all 2 operations are better than 1, if they make in any way for safety, is rather naïve. Our contention is that they do not make for safety, and 2 hospitalizations must be justified to the average patient by substantial evidence, if they are to take the place of 1 operation.

For upward of 25 years the senior author has taught that two basic principles in the operation of thyroidectomy for thyrotoxicosis are: first, that the operation should be thoroughly radical, and second, that it should be done in one stage. By radical operation is meant the removal of all but a minimal amount of thyroid tissue, irrespective of the size of the thyroid. By one stage is meant just what the word indicates, namely, thyroidectomy without preliminary ligation or multiple steps in the operation. The object to be attained is to leave so little thyroid tissue remaining that a postoperative crisis, presumably caused by leaving sufficient thyroid tissue to permit it to occur, cannot follow. In previous papers (10, 12) it was suggested that it was this residual thyroid tissue, thrown into excessive activity by the very psychic and traumatic stimulation of the operation, that was the cause of reactions after operation. In the light of our present knowledge of the part that liver damage with suppression of function plays in thyrotoxicosis, this is undoubtedly oversimplification of the problem. However, the principle remains much the same, since the patient with a highly damaged liver is less able to withstand the effect of the stimulated activity of his residual thyroid. This reaction or crisis is commonly accepted as a major cause of surgical mortality following thyroidectomy for thyrotoxicosis. The practical elimination of crisis as a cause of death should strengthen the basis for the use of a one stage radical operation. If the principle is correct, it should show to the best advantage in the more severe types of cases, such as young children, patients intensely or fulminantly toxic, and the old and infirm with their associated cardiac and other visceral complications. Our results in children and in the aged have been the subject of previous communications by one of the junior authors (J. M., 3). In 1931, Mora and Greene reported 200 consecutive single stage thyroidectomies for thyrotoxicosis in patients over 50 years of age. The present paper presents a further report of thyroidectomy in the aged, consisting of 270 consecutive patients over 50 years of age, operated upon since the earlier series was completed. In all cases the technique previously described (11) was carried out by the senior author. These 270 cases occurred in a consecutive series of 900 patients. It must be emphasized that these operations were for thyrotoxicosis and included cases of primary hyperplastic thyroid and so called toxic adenoma. Non-toxic goiters, nodular or otherwise, are not included.

The degree of illness in these patients is indicated by the fact that 37 of the 270 were decompensated just prior to or at the time of operation. Of these 37 there were 15 who were badly decompensated, 5 of them with marked cyanosis, edema of the legs, abdominal wall, and genitalia, 5 with ascites, and 2 with bilateral hydrothorax in addition. One patient had an aneurism of the aorta associated with a large heart and auricular fibrillation. Four, in addition to thyrotoxicosis and cardiac damage, had an associated severe diabetes and 2 of these were further complicated by hypertension with systolic blood pressures above 200. One was further complicated by acromegaly and profuse sialorrhea. Eighteen of the 270 patients had diabetes of varying severity and 1 was further complicated by a depressive psychosis at the time of operation. One patient was in crisis and 1 exhibited marked mental aberration just prior to preparation for operation; 2 had associated cerebrospinal syphilis, 1 had epilepsy and had had her last attack 6 weeks prior to operation; 1 patient had pernicious anemia.

For any publication such as this, which is essentially a challenge of the idea so widely held, that multiple stage operations in the seriously toxic patient make for a lowering of the mortality, it is necessary that the objective data be such that their value can be estimated and compared easily. Of these we regard the basal metabolic rate as the most valuable for the purpose, not that it takes the place of adequate clinical study, but that the latter is much more subject to the bias of the observer. No data are more fallible, however, than those of the basal metabolic rate when obtained from uncontrolled sources. The patients included in this paper were studied under controlled conditions. Some had first come under observation after receiving iodine preparation. If the patient's condition permitted, the iodine was stopped until adequate

study was possible. A few cases are included in which the patient's condition was such as to make the diagnosis obvious and the interruption of iodine not justifiable. All patients were subjected to the usual clinical study.

Accurate pre-operative basal metabolic rates were obtained in 268 of the 270 patients. The total number of pre-operative basal metabolic rates taken was 861, making an average of 3.2 rates per patient. Two hundred five of the 270 patients had basal metabolic rates above plus 30, and 144 of these had basal metabolic rates of above plus 40. Forty-five of the 65 remaining had basal metabolic rates varying between plus 20 and plus 30. Eighteen had basal metabolic rates below plus 20. Fourteen of these 18 had had previous iodine preparation. Four had clinical manifestations of toxicity and a characteristic response to iodine.

The age of the patients ranged up to 77 years. They included all varieties and all stages of the various complications that one would expect in the aged. Operation was not refused regardless of what complication the patients presented, provided they showed evidence of thyrotoxicosis as well. There were 176 patients between the ages of 50 and 59, 83 between the ages of 60 and 69, and 11 were past 70 years of age, the oldest being 77 years of age.

Weight loss occurred in 147 of the 270 patients. The average weight loss was 25.5 pounds. Loss in weight is necessarily based on the patient's estimate of his previous normal weight and is obviously an approximation only.

Patients, number	Weight loss in pounds
60	20 or less
43	20 to 30
24	30 to 40
12	40 to 50
8	50 to 60

The table shows that 44 of the patients lost more than 30 pounds prior to the operation. The maximum weight loss was 60 pounds within a period of 4 months.

In the old-age group hypertension definitely increases the hazard of thyroidectomy, not only because of the possibility of thrombosis or hemorrhage but because hypertension is often only one of the complications. It may well be associated with decreased kidney function and often these patients have accompanying myocardial damage. In our study 65, or 24 per cent, showed a systolic blood pressure above 170 millimeters of mercury and a diastolic blood pressure above 90 millimeters of mercury; 38, or 14 per cent, showed a systolic blood pressure above 200 millimeters of mercury and a diastolic blood pressure above 100 millimeters of mercury.

Perhaps the most hazardous and most difficult patients to operate upon successfully are those in whom old age is complicated by thyrotoxicosis and cardiac failure. The degree of cardiac failure, the presence of some other associated disease process such as diabetes or hypertension, makes each patient in this group a different and difficult problem.

Clute and Swinton state that 60 of their 145 patients of 60 years or over showed either auricular fibrillation or cardiac failure. Twenty of these 60 showed cardiac failure. Magee and Smith of the Mayo clinic show an incidence of 237 cases of auricular fibrillation out of 504 patients past 50 years of age. They state that among 210 cases of auricular fibrillation associated with hyperthyroidism, cardiac enlargement occurred in 79. In the same group of cases of auricular fibrillation, cardiac decompensation was present in 62.

In our series 120, or 44 per cent, showed some signs of cardiac pathology such as enlargement, auricular fibrillation, or cardiac failure. Auricular fibrillation was present in 48 of the patients. In 27 of these, fibrillation stopped following thyroidectomy. Sixteen continued to fibrillate, being unaffected by thyroidectomy. Fourteen of the 16 were followed from 1 to 8 years, 1 was followed for 10 months after operation, and 1 was followed for 4 months. We have been unable to follow the 5 remaining patients.

Cardiac failure was present in 37, or 13.7 per cent, of the 270 patients. It was of varying intensity but in some instances, as previously indicated, the operative risk was hazardous. Twenty-nine who were followed from 6 months to 4 years showed definite cardiac improvement after thyroidectomy. Of the 8 remaining, 3 who were seen 1 to 2 months

after operation were definitely improved; a fourth patient never returned for study following operation; the fifth patient was improving but died suddenly 2 months after operation; 3 patients were unimproved. These were followed for 2 years, 5 months, and 1 month, respectively.

In the postoperative examination of these 270 patients, 224 were subjected to repeated basal metabolic rate studies. There were 727 basal rates taken, making an average of 3.24 rates per patient. Of those followed 213 had a persistent metabolic rate below plus 15. Eleven had a basal rate above plus 15. Four of these 11 patients had but one postoperative basal rate determination and that within 4 weeks of the time of operation. Three of these 4 could not return for further study. The other one, seen 4 years after operation, was clinically very well, but no basal rate could be obtained. The fifth patient developed a recurrence and was successfully re-operated upon. The sixth patient had a recurrence of toxic symptoms 1 year after operation. Under iodine therapy the basal metabolic rate returned to normal and remained at minus 9, plus 1, and minus 14, the last reading being taken 21 months after operation. The seventh patient had a mild residual thyrotoxicosis with basal metabolic rates of plus 14, plus 26, and plus 21, 1 and 2 years after operation. The 4 remaining patients had unaccountable raised basal rates entirely at variance with the clinical picture. All of them showed an obvious absence of thyroid toxicity during the postoperative follow-up periods of 4, 10, 14, and 18 months, respectively.

Of the 46 patients on whom we did not secure postoperative basal rates, 30 were reported as relieved of their thyrotoxicosis, based on clinical studies by their own physicians. They were followed for 3 months to 8 years. We have been unable to follow the remaining 16 patients because of death, residence in other cities, and failure to co-operate with us. In line with our attitude toward a report of this type, the basal rates obtained by other physicians or at unknown laboratories are not included in this report. Only 2 patients were reported to have had repeated elevated basal rates.

There were 43 patients with clinical hypothyroidism of whom 10 required thyroid substance for 3 years or more. The remainder were easily controlled by small doses of thyroid substance. This group includes 1 patient upon whom a total thyroidectomy was performed for thyrotoxicosis and heart disease.

Attention is called to the fact that this is a rather high percentage of hypothyroidism, but the operation is aimed at keeping the basal metabolic rate at a low level over a fairly substantial period after operation.

Four patients developed reactions after operations. One patient in whom before operation a diagnosis of thyrotoxicosis, diabetes, acromegaly, and damaged heart, had been made, had with these a marked increase in salivation. This sialorrhea was severe enough before operation to require the use of a large box of tissues daily. She developed an enormous edema of the lungs on the first day after the operation and her pulse rate rose to 160. She became comatose for a short while but improved under an oxygen tent and in 48 hours was over the reaction. It was necessary to place this patient in prone position from time to time to help empty the bronchial tree of excessive secretion. This reaction was unaccompanied by toxic symptoms. The second patient's temperature rose to 104 degrees on the second day and receded gradually until by the fourth day the patient was very much improved. The third patient developed a rising temperature and pulmonary edema 36 hours after operation. The temperature rose to 103.4 degrees with associated restlessness and tachycardia. At the end of 48 hours she was in excellent condition. A fourth patient exhibited a rise in temperature to 104 degrees on the day following operation, which was accompanied by auricular fibrillation. Thus only 3 of the 270 patients subjected to one stage thyroidectomy presented thyroid reactions after operation.

There were no deaths in the entire series of 270 consecutive patients reported in this paper. These patients represent the high risk group in thyroid surgery. We feel we must insist that these results justify the principle of the one stage radical operation, and particu-

larly that they raise a serious question as to the propriety of multiple stage operations in any case.

SUMMARY

Two hundred seventy consecutive thyrotoxic patients over 50 years of age were subjected to one stage radical thyroidectomy without a death. During the period in which these patients were operated upon, 900 thyroidectomies for thyrotoxicosis in every age group were performed with 3 deaths, or a mortality of 0.33 per cent. These data are presented as evidence in favor of the routine use of a radical one stage operation for thyrotoxicosis.

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ANOMALIES OF RENAL ROTATION

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THE faulty rotation of ectopic and fused kidneys is well recognized. This paper deals exclusively with the etiology and clinical aspects of anomalous rotation in kidneys which have reached the lumbar level during embryonic development and in which the factor of renal fusion plays no part in accounting for the anomaly. Nineteen cases are included in the present report.

Anomalous rotation is a congenital abnormality which is manifested by an atypical location of the hilum renale. It should not be confused with renal torsion which is an acquired displacement of the entire kidney.

Although an infinite number of intermediate malpositions of the renal pelvis may characterize the derangements of rotation, for the purposes of a clinical classification 4 main types are listed here: (1) ventral or nonrotation (rarely excessive rotation); (2) ventromedial or incomplete rotation; (3) lateral rotation (reverse or excessive rotation), and (4) dorsal rotation (excessive or reverse rotation).

EMBRYOLOGY

The migration of the kidney has been spoken of commonly as a process of ascent and rotation. Hinman has observed, however, that the supposed ascent of the kidney is more apparent than real. The change in position actually takes place because of a more rapid growth of the body, especially the trunk, than of the kidney, this organ occupying relatively the same position in the adult as it does in early embryonic life.

Likewise, as brought out by Priman, it is more rational to view the change in position of the renal pelvis as a manifestation of differential regional growth than as an actual rotation of the kidney. A gradual intrarenal displacement of the pelvis produces the appearance of rotation which does not actually occur. Table I summarizes those details of early human embryonic development which will be considered in interpreting the errors of renal rotation.

It is during the time that the first 5 orders of tubules coalesce to form the renal pelvis that this structure undergoes its medial excursion and the kidney itself makes a pseudoascent out of the pelvis of the embryo. In embryos of 12.5 millimeters (greatest length), the primitive renal pelvis and its first collecting tubules still lie dorsal to the ureter (Fig. 1 A). Shortly thereafter the pelvis commences its ventromedial excursion (Fig. 1 B) and, in embryos of 19.5 millimeters (greatest length), it has assumed the medial position (Fig. 1 C).

The successive orders of collecting tubules are formed by a process of dichotomous branching. Felix has noted that tubules of the second and third order onward usually send out 2 branches ventrally to one in the dorsal direction. Following each division of the ureteral tree, there is a rapid multiplication of cells as the metanephrogenic tissue grows to encase completely the budding tubal stem. Each new ureteral tree and its metanephrogenic cap constitute a malpighian pyramid. These pyramids are marked by grooves which produce a lobulation of the renal surface. The lobulations persist until birth and disappear in the early years, although under some circumstances they persist throughout life.

As described by Felix, the permanent renal circulation is established through the mesonephric arteries at the time the excursion of the renal pelvis is being completed. These arteries arise as transverse branches from the aorta and terminate in the rete arteriosum urogenitale which is a network that lies ventral to the metanephros in the angle formed by the reproductive gland, the mesonephros and the metanephros (Fig. 2).

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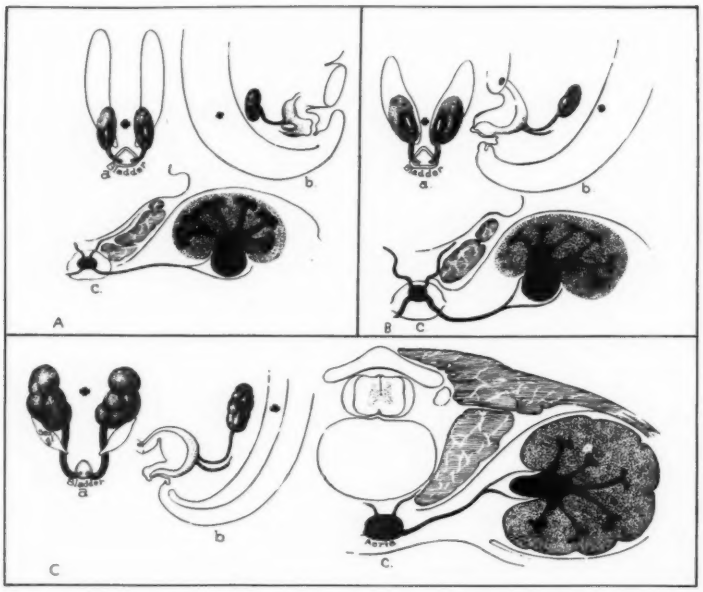


Fig. 1. Diagrammatic representation of the excursion of the renal pelvis, the so called rotation of the kidney. *a*, Ventral view. *b*, Sagittal section through the midline of the embryo. *c*, Transverse section at the level of the second lumbar vertebra, indicated by cross in *a* and *b*. The diagrams show how the kidney retains much the same level in the embryo (the second lumbar vertebra) during this period.

A. Human embryo 12.5 millimeters in length (about 6 weeks old). The renal pelvis and first collecting tubules lie dorsal to the ureter. There is very little metanephrogenic tissue at this stage.

B. Human embryo 16 millimeters in length (about 7 weeks old). The renal pelvis is midway in its excursion to a medial position. Note the lateral dominance of the ureteral trees with the surrounding proliferation of the metanephrogenic tissue producing the medial shift, best seen in *c*.

C. Human embryo 19.5 millimeters in length (about 9 weeks old). The renal pelvis faces the midline at the completion of its excursion. The lines along which the metanephrogenic tissue surround each pyramid begin to form lobulations. Note how the anterior lip of renal parenchyma has curved ventrally around the pelvis.

In embryos of 18 millimeters (greatest length) the network comes into connection with the vessels which actually enter the renal sinus. Normally the vascular pedicle enters the hilum renale ventral to the pelvis at approximately the same time the medial shift is completed. The network makes it possible for any of the mesonephric arteries to become the metanephric artery and also explains the variability in the origin of the renal artery, the frequent dissimilarity on the right and left sides, and their frequent multiplicity. A persistence of more than one of the numerous venous communications similarly accounts for anomalies of the renal vein.

COMPARATIVE ANATOMY

Some animal phyla retain, as permanent excretory organs, kidneys which represent early stages in human embryonic development. It will be shown that the primitive metanephric form found in reptiles and birds closely resembles one of the anomalies of rotation. As seen in the chicken, such a kidney extends far caudad, is lobulated, and presents an embryonic type of pelvis which is located on the ventral aspect (Figs. 3 and 4).

PATHOLOGY

The derangements of renal rotation possess many characteristics which are pathogno-

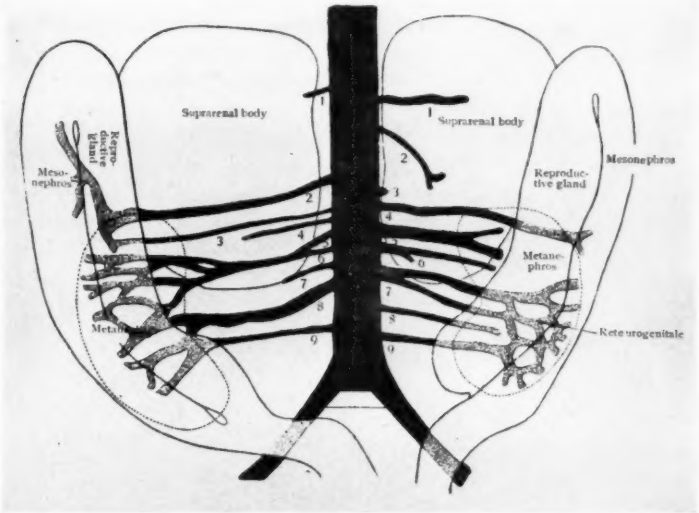


Fig. 2. Diagram showing the manner of renal vascularization. Vessels springing from the aorta form the rete arteriosum urogenitale which lies ventral to the metanephros in the angle formed by the reproductive gland, the mesonephros, and the metanephros. (From Felix.)

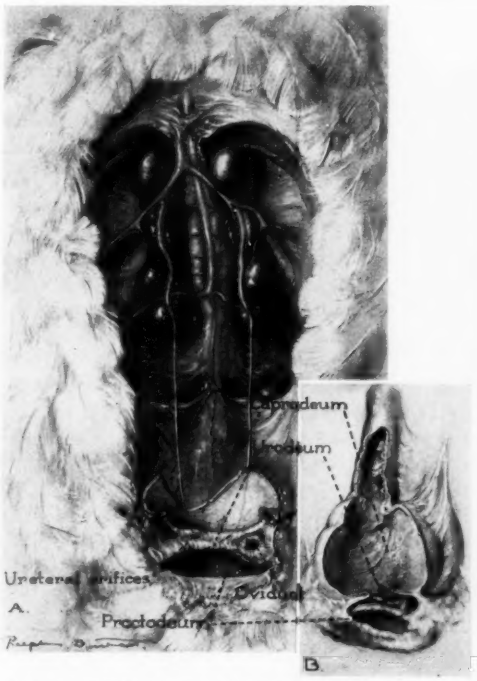


Fig. 3. Primitive type of metanephric kidney as seen in the chicken. The kidneys extend far caudad, lobulations persist throughout life, and the pelvis retains a ventral insertion. The ureters empty into a cloaca, shown in B.

Fig. 4. Pyelogram of chicken. Note the long, narrow, primitive type of embryonic pelvis which gives off abbreviated calyces at regular intervals. Inset: Lateral pyelogram of the pelvis and ureter in a ventral position.

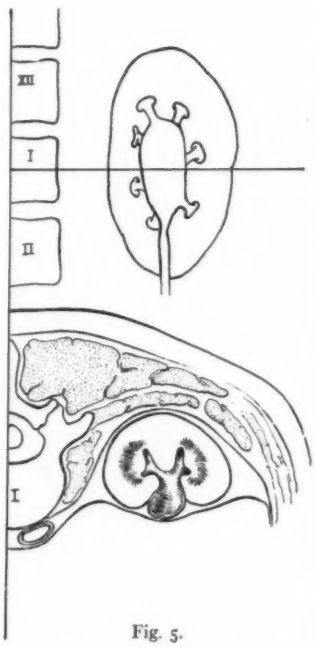


Fig. 5.

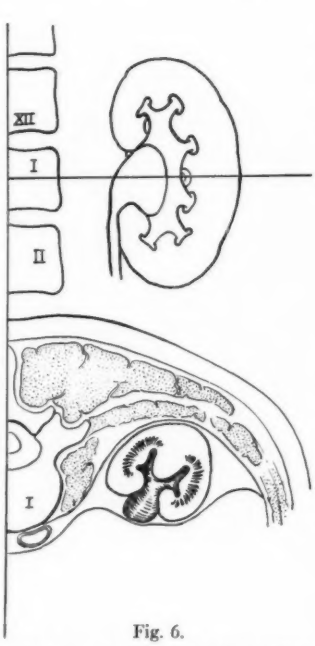


Fig. 6.

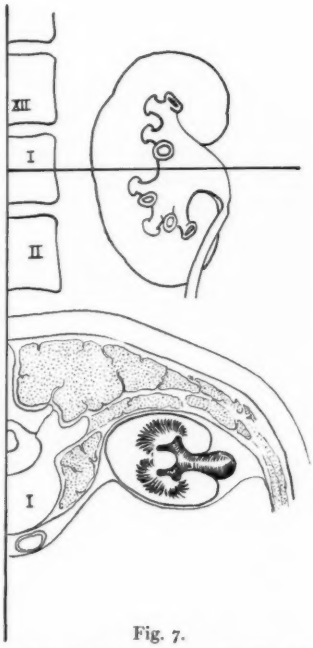


Fig. 7.

Fig. 5. Ventral rotation. Pelvis lies ventral to calyces as seen in early embryonic life. Compare with Figure 1A.
Fig. 6. Ventromedial rotation. The pelvis partially faces the median line of the body. Compare with Fig. 1B.
Fig. 7. Lateral rotation. The pelvis lies lateral to the medially directed calyces.

monic of an arrested or distorted embryonic growth. Most distinctive is the malposition of the hilum renale. In *ventral rotation* the pelvis is situated in its original embryonic position, lying directly ventral to calyces which point dorsally (Fig. 5). *Ventromedial rotation* is a condition in which the pelvis partially faces the midline of the body, lying medial to the dorsolaterally directed calyces (Fig. 6). *Lateral rotation* is manifested by a lateral position of the pelvis (Fig. 7) and *dorsal rotation* by a dorsal insertion (Fig. 8).

A widely exposed renal pelvis is one of the common findings in anomalous rotation (Figs. 9 and 11). In extreme instances there is a complete absence of the hilum renale, the original calyces being separated on the surface of the kidney (Fig. 13).

Although the pelvis may be normal in shape, a distinctive embryonic type is sometimes encountered. Such a type exhibits lengthening and narrowing of the pelvis, abbreviated calyces often clubbed being given off at more or less regular intervals (Fig. 15). Again, the calyces as well as the pelvis may be elongated (Fig. 19) or an elongated cephalic calyx may be a distinguishing feature (Figs. 16 and 17). In some cases the pelvis is ensheathed in broad layers of adherent fibrous tissue which fix the pelvis and contiguous ureter to the adjacent surface of the kidney and peritoneum (Figs. 9, 11, and 13). There may be a lateral displacement of the upper third of the ureter, which is most extreme in lateral rotation (Figs. 10, 14, 15, 17, and 19).

Another characteristic is a discoidal shape of the kidney. As compared to the normal, such a member is either oval or roughly triangular in shape and exhibits an anteroposterior flattening (Figs. 9, 11, 17, and 20). The persistence of fetal lobulations may also complicate the errors of rotation (Figs. 11 and 18).

The blood supply is subject to wide variations. Sometimes an artery and vein discharge

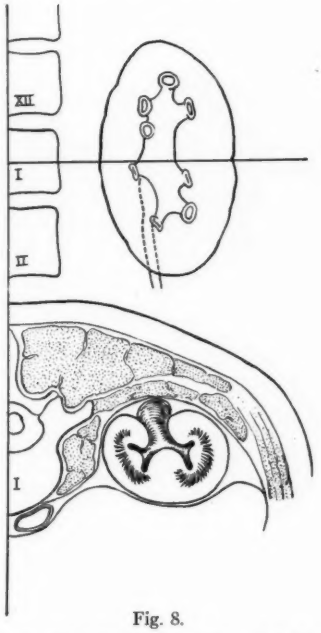


Fig. 8.

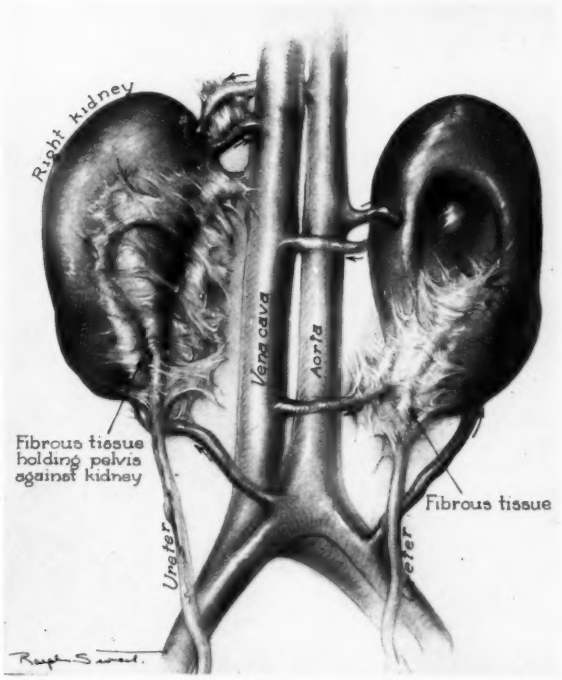


Fig. 9.

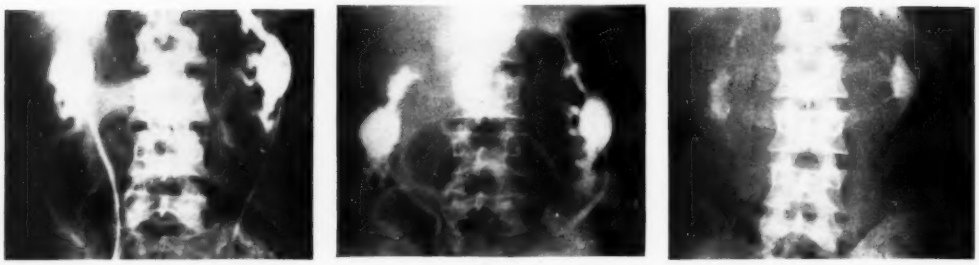
Fig. 8. Dorsal rotation. The pelvis lies on the dorsal aspect of the kidney behind ventrally directed calyces.

Fig. 9. Bilateral ventral or non-rotation (Case 8) as seen at operation. Note the discoid shape of the kidneys, the widely exposed, dilated pelves, and the aberrant blood vessels piercing sheets of fibrous tissue which fix the upper portions of the ureters and the pelves to the parenchyma of the kidney and the peritoneum. The artery and vein entering the superior aspect of the right kidney are typical polar vessels. (See Figure 10 demonstrating bilateral ventral rotation.)

branches through the hilum renale in the normal manner (left kidney, Fig. 11). In other instances the organ is completely supplied by aberrant vessels which are distributed to the parenchyma at points distant from the hilum (Fig. 9). The most frequent termination is at one pole or the other, the vessels being known as polar vessels (Figs. 11 and 20). Finally, aberrant vessels may be present in conjunction with a normal artery and vein (Figs. 11, 18, and 20). Before entering the kidney the vessels are often found to penetrate fibrous bands such as have been described (Figs. 9 and 11). In coursing over an expanse of parenchyma, they commonly lie in a channel of variable depth which has been hollowed out along the path of the vessel (Fig. 13). The entrance of the vascular pedicle dorsal to the renal pelvis may be the sole feature which identifies ventromedial rotation from the normal (right kidney, Fig. 11). From a physiological standpoint the anomalies of rotation demonstrate no impairment of function unless complicated by such factors as obstruction or infection.

ETIOLOGY

As a starting point in deciphering congenital anomalies Bremer suggested that, "An embryological explanation of any anomaly should show that from some pre-existing embryological condition both the normal and abnormal results may be derived; the agents which cause the anomaly should be simple in themselves, as pressure or the blocking of a vessel, or the relative overgrowth or arrest of development of certain parts, though the ultimate cause of these agents will usually remain



A B C

Fig. 10. Pyelograms demonstrating bilateral ventral rotation (Case 8). Note the bilateral hydronephrosis. A, Recumbent pyelogram before operation; B, upright pyelogram before operation, revealing bilateral nephroptosis; C, upright pyelogram following bilateral nephropexy and ureterolysis. The anomalous rotation has been maintained. It will be noted also that the nephroptosis is no longer present.

a mystery. Not infrequently other vertebrates may develop normally in ways which for man would be abnormal, the citation of such instances strengthens the explanation of any human anomaly."

The investigations of Spemann further illuminated the approach to these problems by the recognition of organizing influences and chemohormonal as well as purely mechanical explanations for the processes of growth, both normal and abnormal.

Assuming a normal ventral insertion of the primitive renal pelvis, one may hypothesize on the 4 following errors of pelvic excursion in accounting for the derangements of renal rotation:

1. Non-rotation. A failure of any attempt toward an excursion in either a medial or lateral direction logically explains the condition found in ventral or non-rotation. The pelvis maintains its original embryonic position (Fig. 1 A), similar to the normal arrangement in some species of reptiles and birds (Fig. 3).

2. Incomplete rotation. An interruption of the pelvic excursion at approximately the stage of the seventh embryonic week, at some point midway in the normal medial shift (Fig. 1 B) gives rise to the ventromedial deformity.

3. Excessive rotation. A prolongation of the excursion of the pelvis beyond its normal medial location may result in an anomaly of dorsal rotation, lateral rotation, or in extreme instances, in one of ventral rotation, the pelvis making a circuit of 190 degrees, 270 degrees, or 360 degrees, respectively, from its original position.

4. Reverse rotation. A shift in the direction opposite to the normal could account for the position of the pelvis in lateral rotation or dorsal rotation, the circuit being one of 90 degrees or 180 degrees, respectively.

Clinically it is impossible to differentiate types of reverse rotation from those of excessive rotation. At operation or necropsy, however, a clue to the direction of the pelvic excursion may sometimes be obtained by ascertaining the course of the vascular pedicle. As has been described, the kidney forms its blood supply from the mesonephric vessels which pass ventral to it (Fig. 2). When the pelvis makes a prolonged anomalous excursion, it is likely that permanent vascularization will be established at some time before the pelvis comes to rest.[1] In such an event it has been observed that the pelvis draws along any closely associated vessels in the direction of its circuit. Having an original insertion in the ventral or ventromedial aspect of the kidney, therefore, the main renal vessels will pass ventral to the kidney in reverse rotation and dorsal to it in excessive rotation. Unfortunately, the presence of a completely aberrant blood supply may prevent the application of this principle.

[1]Bremer contended that endothelial sprouts will not pierce condensed mesenchyme and that the presence of a very slightly differentiated capsule around an organ will protect it from future ingrowth of blood vessels. This factor would be a compelling influence in the maintenance of early vascularization.

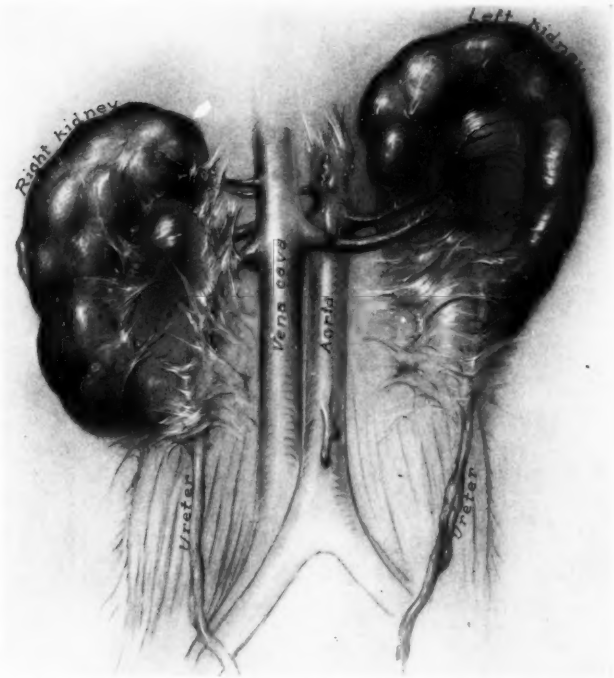


Fig. 11. Left ventral rotation and right ventromedial rotation (Case 11) as seen at operation. Note the widely exposed, hydronephrotic pelves, the lobulations of the renal parenchyma, and the fibrous bands fixing the pelves and upper portions of the ureters to the parenchyma of the kidney and peritoneum. On the right, polar vessels enter the superior pole. The main vascular pedicle passes dorsal to the pelvis, establishing the diagnosis of ventromedial rotation. Both groups of vessels pierce bands of fibrous tissue in supplying the kidney. (See Figure 12.)

The ventral course of the blood vessels in Case 19 (Fig. 13) gives evidence of a reverse excursion of the pelvis in attaining the position of lateral rotation. On the other hand, in Case 16 (Fig. 18) the dorsal course of the renal artery and vein indicates an excessive excursion of the pelvis. Labey and Paris described a kidney in the position of ventral rotation in which the main vascular pedicle passed dorsal to the kidney before it entered the hilum lateral to the pelvis (Fig. 20). This pathological relationship plainly indicates that the pelvis made a complete circle of 360 degrees in the normal direction before coming to rest in its original ventral position. The mechanism is, therefore, one of excessive rotation.

Such instances of a total disregard for neighboring vessels as either anchoring agents or hindrances to the excursion of the pelvis indicate that the factors influencing the pelvic shift are independent of those which control vascularization. It is improbable, therefore, that an anomalous vascularization or one that is premature or delayed—either normal or anomalous—could play any rôle in accounting for the errors of rotation.

This view gains additional support from observations on the manner of vascularization in the normal embryo. When the testis is formed in the lumbar region, for example, it is not fixed there by its vascular communications with the aorta and inferior vena cava or left renal vein. Quite unimpeded, as the

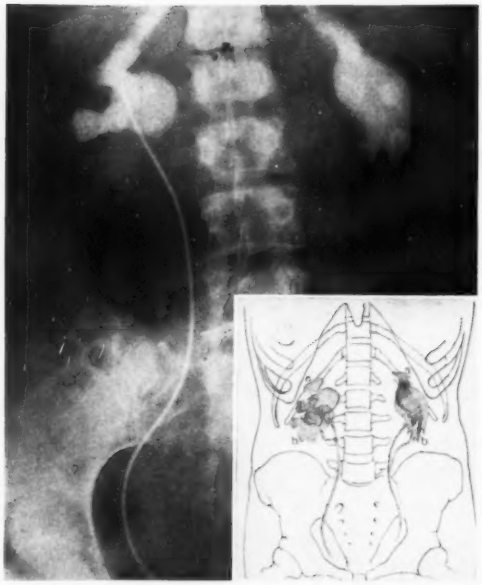


Fig. 12. Pyelogram demonstrating left ventral rotation and right ventromedial rotation (Case 11). Note the bilateral hydronephrosis. Inset shows *a*, the recumbent position, *b*, the upright position. (From Hinman.)

trunk lengthens, the organ makes its journey to the scrotum, carrying along its blood supply as it goes. For these reasons one questions the hypothesis that is forwarded in many urological texts that the abnormal position of ectopic kidneys is determined by anomalous vascular attachments. It seems to me that vascularization is secondary to other more powerful forces which regulate the form, position, and relationship of organs.

The conception of rotation as an intrarenal excursion of the pelvis invalidates those mechanical theories which attempt to explain normal and faulty rotation on the basis of extrarenal forces. It becomes necessary, therefore, to scrutinize such intrarenal forces as might produce rotation. Let us first consider the ureteral tree as the prime motivating agent in the formation of the kidney. Spemann showed that certain embryonic structures, which he termed organizers, possess the remarkable power of causing other embryonic tissues to differentiate or "organize" in a particular manner. What evidence points to the ureteral tree as the organizer of the renal blastema in metanephric development?

Boyden performed a series of experiments which clearly proved that the nephrogenic component of the kidney does not grow in the absence of the ureteral component. By destroying the distal ends of the wolffian ducts in chick embryos, he successfully prevented the formation of a ureteral bud in many instances. Although the renal blastema invariably appeared subsequently even in the ab-

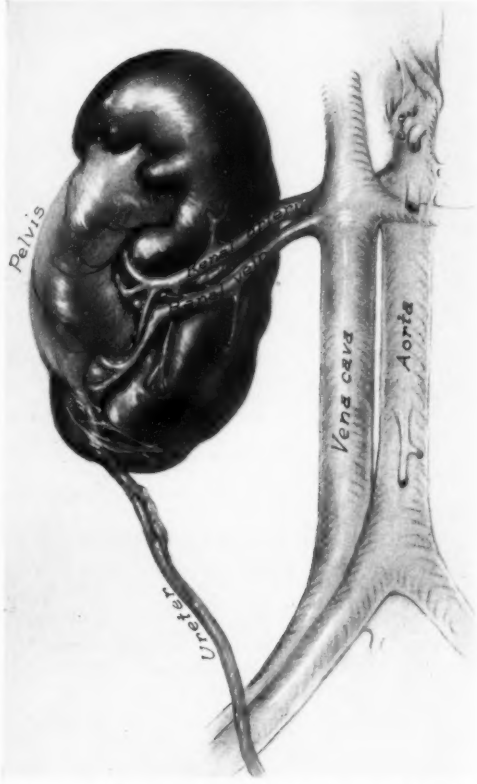


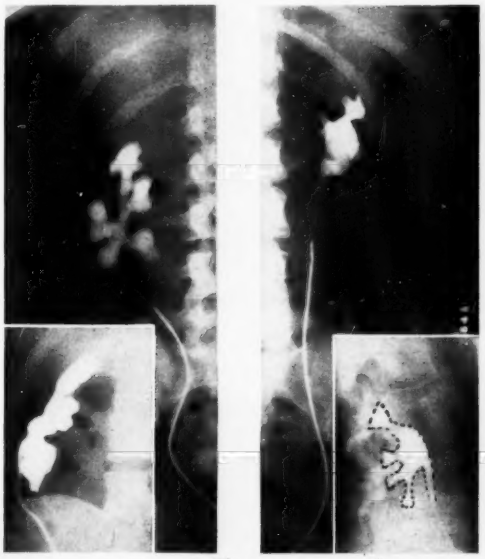
Fig. 13. Right lateral rotation (Case 19) as seen at operation. Note the dilated pelvis and original calyces exposed on the renal surface. The vascular pedicle lies in a groove formed in the ventral aspect of the parenchyma giving off tributaries along its course. This ventral location of the pedicle establishes the anomaly as one of reverse rotation. A few fibrous bands fix the upper portion of the ureter to the parenchyma at the lower pole. (See Figure 14.)

sence of the ureteral elements, there was no differentiation into secretory tubules, and a lessening density predicted its eventual disappearance. In studying a human embryo 10 millimeters in length, Boyden found tubules being formed in a normal right blastema but no evidence of such activity in the left blastema which lacked a ureter.

Nicholson made the pertinent observation that the ureter precedes and, therefore, controls the blastema in differentiation. He further stated that there is on record no case of ureteral agenesis in which there was a mass that might represent renal blastema. If the renal blastema were self differentiating in the absence of a ureteral bud, one would expect to find some mass, most likely cystic, at or near the level of the bifurcation of the aorta.

Fig. 14.

Fig. 14. Pyelogram showing right lateral rotation and mild hydronephrosis (Case 19). Note the lateral displacement of the upper third of the ureter.



a Fig. 15. b

Fig. 15. a, Right ventral rotation (Case 7) confirmed by right oblique lateral pyelogram (inset) and at operation. Note the elongated, embryonic type of pelvis giving off clubbed, abbreviated calyces at fairly regular intervals. b, Left ventral rotation (Case 3), proved by left oblique lateral pyelogram (inset). The calyces in this instance are not clubbed and the pelvis more closely approximates the normal conformation.

Fig. 16.

Fig. 16. Pyelogram demonstrating left ventral rotation (Case 5) as established by a left oblique lateral view (inset) which shows the pelvis directly ventral to the calyces. Note the embryonic type of pelvis with the distinguishing elongated cephalic calyx.

Fig. 17. Bilateral ventral rotation (Case 9). Pyelograms show the pelves lying in the midportion of disc-shaped renal outlines. Lateral views established the ventral location of the pelves. Note the lateral displacement of the upper portion of both ureters and the elongated cephalic calyx on the left.

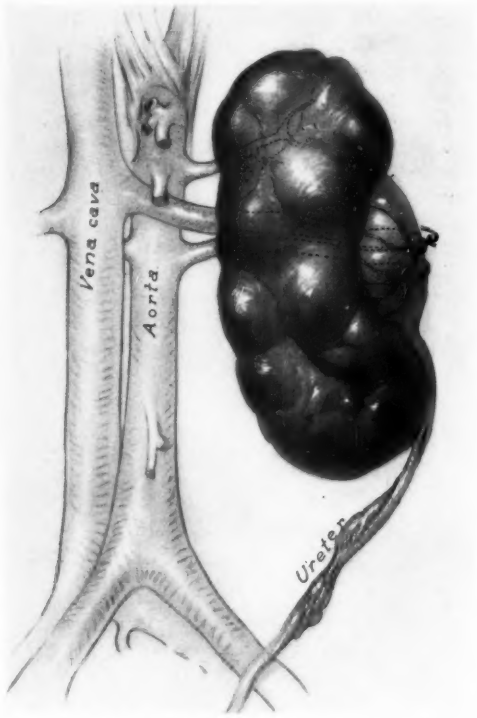


Fig. 18. Left lateral rotation (Case 16) as seen at operation. The main vascular pedicle passes dorsal to the kidney in order to enter the hilum, thereby indicating an etiology of excessive rotation. Note the lobulations and the aberrant artery to the upper pole. (Courtesy of Dr. J. F. Luten). (See Figure 19.)

Further weight is lent to this conception by the work of Brown who discovered an inherited factor of retardation in renal development following radiation of a strain of mice. In order to form a functioning kidney, she found it absolutely necessary that the ureter penetrate the blastemic mass. Brown explained retarded ureteral growth on the basis of a deficient or unbalanced germplasm. In making tissue cultures Drew observed that, although pure renal epithelium grew as undifferentiated sheets, the addition of connective tissue induced differentiation and the formation of rudimentary tubules.

Previous note has been made of the manner in which the nephrogenic tissue organizes around each branching of the tubal stem during normal metanephric development. All of these facts speak strongly for an activating or organizing power inherent in the ureter.

Priman emphasized that at the time of rotation the ureter branches very rapidly. After providing this valuable clue toward solving the intricacies of rotation, however, he reverted to a mechanistic explanation. He claimed that the divisions of the primary renal pelvis grow more easily in the lateral and especially in the ventral direction because the growth in the dorsal and medial directions is limited by dorsal body wall. This belief seems untenable when one studies cross sections of embryos during this period. Figure 21 (taken from Felix), representing a human embryo 19.4 millimeters in length, shows that well through the stage of pelvic excursion the metanephros is surrounded by the loose mesenchyme of the retroperitoneum on its dorsal, medial, and lateral aspects.

It seems more logical to attack the problem by assuming that renal ascent and rotation

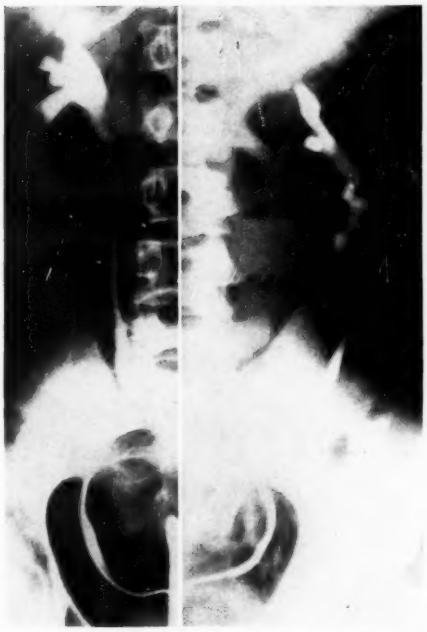


Fig. 19. Pyelogram showing left lateral rotation (Case 16). Note the elongation of the renal pelvis which suggests a renal tumor. The ureter is displaced laterally in its upper third. (Courtesy of Dr. J. F. Luten.)

Fig. 20. Right ventral rotation attended by an excursion of the pelvis of 360 degrees in the normal direction as indicated by the dorsal course of the main vascular pedicle. The mechanism is one of excessive rotation. Note the triangular, flattened, discoid shaped kidney. Two groups of polar vessels are seen. (After Labey and Paris.)

represent characteristics of a higher type of kidney. The mammalian kidney is advanced over the primitive metanephros seen in some vertebrates, such as the bird (an off-shoot of man's family tree), by a more complicated ureteral development, manifested in part by a more fully developed pelvis which undergoes a medial excursion.

Granting that the pelvic excursion is a manifestation of advanced renal development, how is it brought about? Mention has been made of the manner in which tubules of the second and third order onward send out 2 branches ventrally to one in the dorsal direction (Fig. 1B, *c*). When one considers how the elaborate ingrowth of metanephrogenic caps follows each successive division, this factor of excessive ventral branching contributes the first step toward explaining the change in the position of the pelvis.

A medial instead of a lateral movement of the pelvis is best explained by a process of dichotomy and lateral dominance as applied to the ureteral tree. As a predominantly horizontal dichotomous branching takes place, lateral dominance influences a lateroventral growth of successive orders of tubules with an inevitable medial shift of the pelvis. Figure 22 (taken from Felix), a model of the right ureteral tree of an embryo 19.4 millimeters long shows how the early orders of tubules curve medially around the pelvis (also see Fig. 1C, *c*).

A vicarious or reverse excursion of the pelvis would result from a transference of the lateral to a medial dominance. An analogous transference is common in other organs of the body. Spemann and Falkenberg, for example, traced various stages of a transposition of the thoracic and abdominal viscera to a transference of the normal dominance of the right half of the blastoderm to an abnormal dominance of the left half. Either partial or complete transference may take place.

The infinite possibilities afforded by various degrees of transference of dominance, or by a deficiency or excess of those factors producing

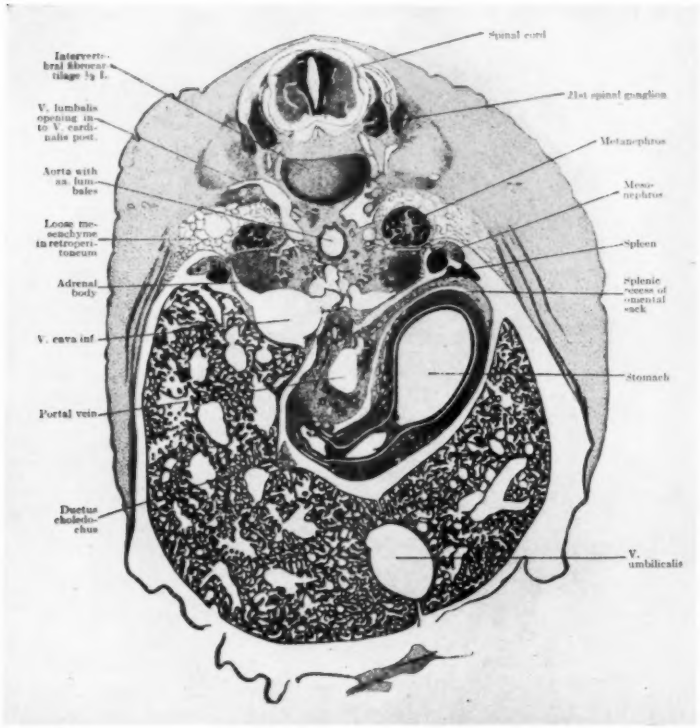


Fig. 21. Cross section of a human embryo 19.4 millimeters in length showing the metanephros lying in the loose mesenchyme of the retroperitoneum. Note the relatively enormous size of the liver at this stage. (From Felix.)

dominance could account for every possible type of anomalous renal rotation. The ultimate causes of these changes are still undefinable, although from the experimental data so far available they have been variously expressed as alterations in germplasm, in hormonal activity, or in metabolic activity, or have been attributed to variations in the chemical structure or the temperature of the tissues at organization centers.

Apart from a faulty excursion of the pelvis, an entirely different etiology must be considered as the possible cause of dorsal and lateral rotation. A late insertion of the ureter on an atypical aspect of the renal blastema is well within the realm of possibility. At the time of the appearance of the ureteral bud the mesonephros and liver are undergoing rapid proliferation (Table I). The rapid expansion of these comparatively large intra-abdominal organs results in a considerable widening of the abdominal region in the embryo and a lateral displacement of the wolffian ducts during a critical stage in renal development. Should the ureteral bud make a late appearance, it would arise from a more lateral position than usual. In the event of a delayed union with the renal blastema both components would be older and a permanent anomalous position of the renal pelvis might result. This circumstance might also arise from an abnormally high budding of the ureter from the wolffian duct.

The anomalies of renal rotation are common to both sexes; 13 males and 6 females comprised this series. In age, the patients ranged

TABLE I.—STAGES IN EARLY HUMAN EMBRYONIC DEVELOPMENT OF THE PRONEPHROS, MESONEPHROS AND METANEPHROS

Embryo		Pronephros	Mesonephros	Metanephros	Renal vessels	Liver
mm.	weeks					
1.7		Appears				
2.5		Growth	Appears			Appears
4.5 to 5.3		Degenerates	Rapid growth	Appearance of ureteric bud and renal blastema which lies medially		Extensive proliferation of cells in lateral and ventral walls
7	5			Metanephrogenic cap (blastema) grown around ureteric bud		Liver continues to grow rapidly
8.5 to 9.5	5			Ureter grows cranially into retroperitoneum		
9.5 to 13	5 to 6			Ureteric bud halted by outgrowing collecting tubules of 1st order establishing definitive level of renal pelvis in foetus (2nd lumbar vertebra)	Mesonephric arteries take origin as transverse branches of aorta. Formation of terminal network—rete arteriosum urogenitale	
12.5 to 19.5	6 to 9		First period of degeneration	*Medial rotation of pelvis:* 12.5 mm.: pelvis and 1st order of collecting tubules dorsal to ureter. 19.5 mm.: ureteric tree lateral to pelvis. Formation of collecting tubules up to 5th and 6th orders.	18 mm.: network comes into connection with vessels entering renal sinus. Vessels of metanephros thus connected by mesonephric arteries to aorta.	
21 to 30	10		First period of degeneration completed at 21 mm.	Some observers place completion of rotation at 30 mm. (Priman)	21 mm.: mesonephric artery destined for metanephric distinguished from its fellows by a greater diameter	
			Second period of degeneration			
70				Actual capsule of kidney first distinctly seen at 70 mm. Formation of collecting tubules of 9th, 10th and 11th orders		

from 16 months to 53 years, the average age being 29 years at the time the condition was recognized. The incidence of the various anomalies is listed in Table II. No case exhibited dorsal rotation[1] although Campbell has seen 2, and Papin a number of cases of this type. There is apparently no predilection to either the right or the left side, the right being affected 10 times and the left 13 times.

SYMPTOMS

Uncomplicated derangements of renal rotation give rise to few, if any, symptoms (Table II). A dull, aching, homolateral pain in the lumbar region is the most constant complaint. One patient having a right ventromedial deformity, complicated by infection and hydronephrosis, experienced pain in the right upper abdominal quadrant which completely disappeared following nephrectomy. Hematuria is occasionally observed. The bleeding, which varies greatly in amount, can be traced universally to the affected kidney. Other symptoms are caused by some asso-

[1]Since this paper was submitted for publication a case of left dorsal rotation came to necropsy at the University of California Hospital. A brief report of the findings is here appended through the courtesy of the Department of Medicine.

The patient, a white male 43 years of age, succumbed to aleucemic lymphatic leucemia. He had given no history of any urinary disturbance and had presented no symptoms which would direct attention to the anomaly. During his hospital stay the urine was found to contain a few red blood cells, but no pus cells or organisms.

At necropsy both kidneys were found in the usual lumbar position and both showed widely exposed calyces which could be traced almost to their insertion in the parenchyma (Fig. 24). The right kidney was normally rotated but the left demonstrated a dorsal rotation. The blood vessels took a dorsal course in entering the hilum of the anomalous member, indicating excessive, rather than reverse rotation. Several cysts about 1 centimeter in diameter were scattered throughout its cortex.

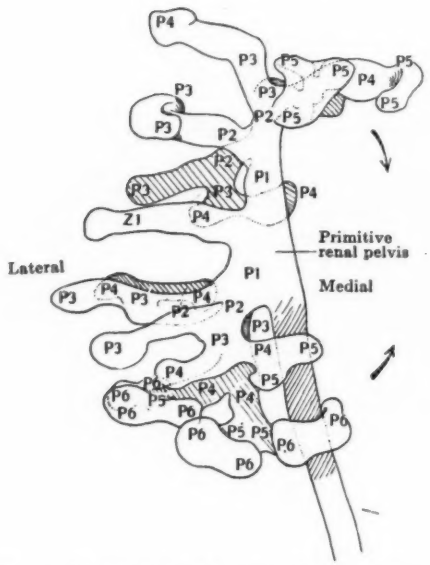


Fig. 22. Model of the right ureteral tree of a human embryo 19.4 millimeters in length, seen from the front at the completion of pelvic excursion. Note the embryonic type of pelvis. The early orders of tubules curve medially around the pelvis in the direction of the two arrows. This mechanism produces the normal medial excursion of the pelvis. *P* and *Z* denote the pole and central tubules, respectively. (From Felix.)

ciated condition. In fact, the numerous complaints which arise from the complications of anomalous rotation often direct attention to the underlying malformation.

DIAGNOSIS

Although it is possible on extremely rare occasions to palpate the hilum renale in its anomalous position in most instances, pyelographic studies are necessary for an accurate clinical diagnosis. While the anteroposterior pyelogram serves to identify lateral rotation (Figs. 14 and 19), the only method of differentiating the types clinically in which the calyces overlie the pelvis is by means of lateral or stereoscopic views (Figs. 15 and 16). The greatest difficulty is encountered in recognizing ventromedial rotation because this anomaly so closely approximates the normal position of the kidney (Figs. 12 and 23).

It is important to distinguish between anomalous rotation and torsion on the longitudinal axis of the kidney. A pyelogram which shows the characteristics of an embryonic pelvis or discloses the presence of one of the obvious causes of torsion, such as a retroperitoneal tumor, facilitates the diagnosis. At operation or necropsy, of course, the distinction can easily be made on the basis of the different pathological features of the 2 conditions.

Bilateral anomalous rotation may be mistaken for horseshoe kidney. The palpation of an isthmus, however, or the demonstration of its presence in the roentgenogram will serve to identify the latter malformation. Ectopic kidneys are easily identified by their abnormal

TABLE II.—ANALYSIS OF 19 CASES OF ANOMALOUS RENAL ROTATION[1]

	Ventral rotation Cases 1 to 11	Ventromedial rotation Cases 11 to 14	Lateral rotation Cases 15 to 19	All types
Number of affected kidneys	14	4	5	23
Symptoms (from affected kidney):				
Dull, lumbar pain	9	2*	3	14
Asymptomatic	3	1	1	5
Chills and fever†	3	1	1	5
Hematuria	1	1	1	3
Dysuria and frequency†	2	0	0	2
Renal colic	1	0	0	1
Complications (each kidney):				
Infection	5	2	2	9‡
Hydronephrosis	5	3	1	9
Nephroptosis	4	1	1	6
Ureteral calculus	1	0	0	1
Treatment (to affected kidney):				
Nephropexy and ureterolysis	4	1	1	6
Pelvic lavage (1 per cent silver nitrate)	3	0	2	5
Nephrectomy§	1	1	0	2
Pyeloplasty‖	0	1	0	1
Exploration of kidney¶	0	0	1	1
Ureterolithotomy	1	0	0	1
Result (each kidney):				
Improved (Follow-up 2 mos. to 5 yrs., average: 8 mos.)	9	3	3	15
Not treated	5	1	1	7
Unimproved	0	0	1**	1

[1]This series comprises 3 cases of bilateral ventral rotation, one combined anomaly of left ventral and right ventromedial rotation and 15 unilateral deformities.

*In one additional case a dull pain was referred to the anterior abdominal wall over the region of the affected kidney.

†From renal infection.

‡Infecting organism: b. coli 6 times, staphylococcus 2 times, proteus in one instance.

§For infected hydronephrosis, extremely poor renal function.

‖For infected hydronephrosis, fair renal function, good return postoperative.

¶The pyelogram suggested a possible renal tumor.

**Case of hydronephrosis and nephroptosis not relieved by nephropexy, underwent a subsequent nephrectomy for persistent lumbar pain at another clinic.

Cases 15 and 17 are included through the courtesy of Dr. W. M. Coppridge and Case 16 through the courtesy of Dr. J. F. Luten.

Fig. 23. Left ventromedial rotation complicated by hydronephrosis and infection (Case 14). Obstruction caused by aberrant artery constricting ureteropelvic junction. The pyelogram so closely resembles that of a normally rotated kidney that the diagnosis was not suspected until the renal pelvis was found located ventral to the vascular pedicle at operation (pyeloplasty).

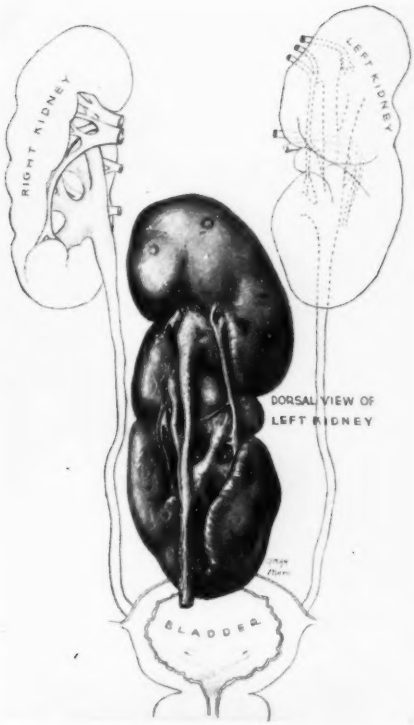


Fig. 24. Left dorsal rotation (necropsy specimen). Note the wide exposure of the calyces of both kidneys. The blood vessels on the left course dorsal to the kidney in entering the hilum, indicating excessive rotation. Several cysts are seen showing through the capsule.

location and short ureters. Baggio called attention to the danger of failing to recognize anomalous rotation when ptosis is present. Finally, the pyelographic picture of elongated, narrow calyces may suggest renal tumor (Fig. 19), or polycystic disease. Lateral displacement of the upper portion of the ureter is another sign which is seen in both renal tumor and anomalous rotation.

COMPLICATIONS

Renal infection and hydronephrosis each occurred 9 times in the 23 anomalies of the present series (Table II). They were associated in 5 instances, and occurred separately in 4 instances. The causative agents producing hydronephrosis were: (1) bands of connective tissue which fixed the upper part of the ureter and adjacent renal pelvis to the renal parenchyma and peritoneum, preventing a free pyelo-ureteral motility, a factor stressed by Herrick, de la Pena, and Raguz; (2) the compression of the ureteropelvic junction by an aberrant blood vessel; (3) congenital stricture of the ureteropelvic junction; and (4) nephroptosis producing an angulation of the ureteropelvic junction. The combined factors of nephroptosis and fibrous bands contributed to hydronephrosis in 4 instances, nephroptosis alone in 2, aberrant blood vessels in 2, and congenital stricture in 1 instance. The presence of a ureteral calculus complicated one case of non-rotation, the malformation being discovered on pyelography. Dr. A. Vitale, in 1930, reported the uncommon coincidence of tuberculosis and renal tumor in anomalous rotation.

Strangulation may be a more frequent complication of the anomalies of rotation than is generally suspected. The renal bleeding in these conditions has never been satisfactorily explained. An area of strangulation, too mild to evoke any symptom other than hematuria, could well be produced by a transient compression or angulation of one or more of the frequently associated aberrant blood vessels. Although severe, recognizable degrees of strangulation may occur in faulty rotation, as in Westerborn's patient, the acute condition is more often encountered in renal torsion.

PROGNOSIS

Anomalous rotation is an abnormality which is entirely compatible with a healthy existence. As is true of any congenital renal malformation, however, there is an increased incidence of dangerous complications (Table II), such as obstruction and infection. The prognosis rests largely upon the nature and severity of these complications, being better for a unilateral than for a bilateral anomaly. In the present series no fatality occurred although one patient was critically ill from a bilateral hydronephrosis complicating bilateral non-rotation (Case 8).

TREATMENT

When unassociated with other renal abnormality, the treatment of the errors of rotation is chiefly symptomatic. Some cases are discovered accidentally, as during the investigation of the opposite kidney, and require no treatment. Relief from renal bleeding is usually afforded by pelvic lavage with 0.5 to 1 per cent silver nitrate, physiological serum mixed with adrenalin, or 30 per cent sodium iodide. Rodriguez and Ajamil reported success following the use of the 2 latter solutions. When pain over the region of the kidney is a persistent symptom, nephropexy combined with pelvo-ureterolysis may be carried out with a good expectancy of relief. Renal sympathectomy may also prove helpful, although in the absence of a normal vascular pedicle it may be impossible to identify the sympathetic plexus.

Pyelonephritis, occurring in the absence of obstruction, should be treated conservatively. Hydronephrosis may be relieved by some form of plastic operation on the pelvis, as in Case 14 and that reported by Moore, by pelvo-ureterolysis, or by nephropexy, depending upon the etiological factor. For advanced hydronephrosis, however, nephrectomy is indicated provided the function of the opposite kidney permits (Cases 10 and 13). Acute renal strangulation, as evidenced by a painful mass in the region of the kidney, hematuria, nausea, vomiting, and shock requires immediate exploration. If the normal color of the organ is restored by relieving the torsion, nephropexy becomes the operation of choice. In the presence of gangrene nephrectomy is imperative.

It is essential that the surgeon be familiar with the pathological characteristics of the anomalies of rotation. A knowledge of the position of the pelvis obtained before operation will determine and facilitate the approach and eliminate needless manipulations. No aberrant blood vessel should be divided without preliminary compression in order to ascertain that it may be sacrificed without endangering the vitality of the kidney. If a wide area of discoloration appears on the renal surface following this maneuver, the vessel must be preserved. The importance of freeing the renal pelvis and ureter from adherent fibrous bands and peritoneum is obvious. In performing a nephropexy, the anomalous rotation, if deviating to any marked degree from the normal, should be retained (Fig. 10); for, in most instances the conversion of this anomalous rotation to the position of a normal kidney would produce torsion of the ureter, displace adjacent intraperitoneal viscera, and require the division or angulation of important blood vessels.

SUMMARY

1. The anomalies of renal rotation, exclusive of ectopic and fusional deformities, may be divided into 4 main types: (1) ventral or non-rotation (rarely excessive rotation); (2) ventromedial or incomplete rotation; (3) lateral rotation (reverse or excessive rotation); (4) dorsal rotation (excessive or reverse).

2. The change in the position of the hilum renale which takes place during early embry-

onic life results from a differential regional growth within the metanephros rather than from an actual rotation of the entire organ.

3. Hypotheses concerning the etiology of anomalous rotation are advanced, emphasis being placed on such intrarenal forces as the organizing activity of the ureteral tree as opposed to any extrarenal mechanical influence.

4. The clinical aspects of the condition are discussed and 19 cases summarized.

I wish to express my appreciation to Dr. Edwin P. Alyea, Dr. Frank Hinman, and Dr. John B. deC. M. Saunders for their valuable assistance in the preparation of this paper.

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INTRACAPSULAR FEMORAL NECK NON-UNION

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IN 1822, Sir Astley Cooper in his book on fractures and dislocations, stated that he had seen only one femoral neck fracture heal by bony union. This reluctance to bony union has been noted by all subsequent investigators of the subject, each believing he had an added feature which would mitigate such a tendency. Many and varied methods have therefore been produced for treatment of the fresh femoral neck fracture, all with their adherents, each with its failures. These failures bring the femoral neck non-union harshly to our attention and, like its predecessor, the methods for its treatment are many and varied. The designation of the problem by Kellogg Speed as the "unsolved fracture" is very appropriate.

Several factors have definite bearing upon the development of pseudo-arthrosis in this area. Of primary importance is incomplete reduction of the fracture which occurs either as a result of interposition of soft tissue as synovia or capsule, or because of physical inability to appose and maintain apposition of the fracture surfaces for an adequate period of time. With the present use of lateral roentgen views of the hip this factor should be minimal. Of secondary importance is the disturbance of the blood supply to the femoral head. From the studies of many workers, the view has been accepted that this blood supply is threefold; first, through the ligamentum teres, the arteries of which have been shown (4, 19) to be of sufficient size in many individuals to be of some value; second, through the femoral neck vessels; third, from the capsular branches of anterior and posterior cervical arteries. Following an intracapsular fracture, the head fragment depends entirely upon the supply through the ligamentum teres. Two possibilities follow: The blood supply may be sufficient to maintain the tissues of the head in a living condition, in which case the head fragment undergoes atrophy of disuse equal in intensity to that of the surrounding bone. If reduction of the fracture had occurred previously, both fragments contribute to callus formation. Should the blood supply be insufficient, the tissues in the head of the femur undergo death and aseptic necrosis (12, 14) unless the blood supply becomes re-established. Impaction of fragments probably plays a part in early entrance of new vessels into the head fragment. A re-attachment of capsule to the head would also be desirable. In any event, many head fragments undergo necrotic changes which are manifested on roentgenograms in 4 to 6 weeks by the apparently increased density of the head as compared to surrounding bones which have undergone atrophy of disuse. This apparent increased density is merely the retention of original density as removal of calcium necessitates efficient circulation. Of last consideration is disturbed osteogenesis. Periosteal callus, so desirable in all fractures, is not available as the intracapsular portion of femoral neck is devoid of periosteum. Phosphotase values may be altered, disturbing bone healing. Neighboring cortical aseptic necrosis may be unusually marked, deferring onset of healing until these areas are replaced by creeping substitution. The detergent action of synovial fluid on proper development of the callus is mentioned only as a possibility considered by very few authorities.

Thus it is evident that some fractures fail to unite even under the best management and under any method of treatment. Definite questions arise. Is it possible to determine this tendency to non-union sufficiently early to relieve the individual of prolonged treatment? What is the procedure to employ in the case at hand?

The clinical picture seems discouraging. The mortality following fracture is given at 20 to 25 per cent. Under the closed methods of treatment, 60 per cent of the remainder obtain bony union. Thus, with failure to ob-

From the University of Nebraska College of Medicine.

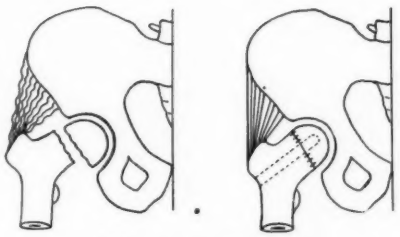

Fig. 1. Albee bone graft.

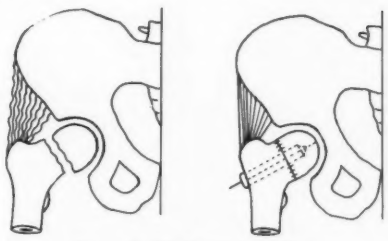

Fig. 2. Smith-Petersen nailing.

tain bony union after 3 or 4 months in a hip spica cast, a bone graft is placed across the pseudo-arthrosis and a similar period of rest in a cast follows. This procedure may also fail, and in this event a new joint is then constructed or an osteotomy performed, thereby changing the static stresses. All of these new joints are very prone to develop degenerative changes with associated pain and hence the problem may persist. In desperation, the hip joint may finally be fused surgically with production of a stable, painless, weight-bearing hip, but only after the individual has been under active surgical treatment of almost 2 years' duration.

Should we choose a line of conduct with union in view, reconstruct the hip joint, or perform a palliative procedure?

The Albee bone graft following open reduction, a major maneuver, presents technical difficulties as illustrated by the differences reported in favorable end-results. Bony union is obtained in 90 per cent of cases in the hands of the originator of the bone graft method (1), probably because of his efficiency and dexterity (Fig. 1). Other surgeons (3, 8) report only 70 to 75 per cent favorable results. The original trauma of injury plus the subsequent operative trauma would predispose to degenerative changes about the head. The long immobilization necessary would certainly aggravate any pre-existing degenerative arthritic changes, and such a finding would seem to be a contra-indication to the bone graft procedure.

Open reduction and fixation with the Smith-Petersen nail is associated with less trauma but the nail produces at least a slight degree of tissue reaction (Fig. 2). With severe atrophy of the head fragment, absolute fixation is impossible, hence such a finding would predispose to increasing varus and pin extrusion. With necrosis of the head, crushing or fracture may occur from the impacts sustained while inserting the nail. In any event, the nail would be able to contribute nothing but fixation whereas a bonegraft would aid in early revascularization.

In the Whitman reconstruction (18), the head fragment is sacrificed, the neck re-shaped to fit the acetabulum and the greater trochanter with attached abductor muscles is transplanted to a new bed lower down in the shaft, thus maintaining the gluteus medius and minimus muscle groups in good tone for subsequent active abduction (Fig. 3). The Albee reconstruction consists of similar reshaping of the neck to fit the acetabulum, the lateral portion of the upper 3 or 4 inches of the femoral shaft and greater trochanter with attached abductor muscles being wedged outward and the angle maintained by a wedge formed from the sacrificed femoral head as shown in Figure 4.

The Colonna procedure (5) places the top of the greater trochanter with a small amount of attached tendinous tissue into the ace-

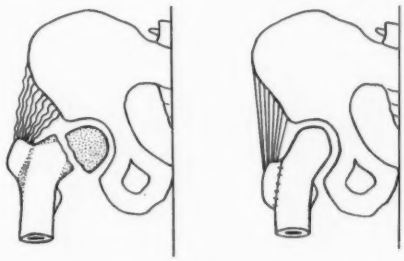

Fig. 3. Whitman reconstruction.

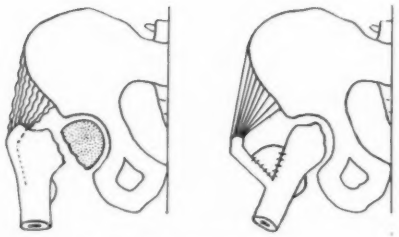

Fig. 4. Albee reconstruction.

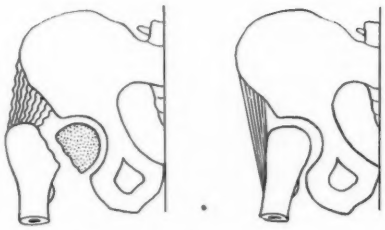

Fig. 5. Colonna reconstruction.

tabulum, the abductor muscles being anchored in a bed lower down on the shaft (Fig. 5). Magnuson implants the reshaped neck in a bed in the head, and also transplants the greater trochanter with attached muscles lower (Fig. 6). Brackett places the proximal end of the distal fragment of an intertrochanteric osteotomy into a similar bed in the head (Fig. 7). As all of these reconstructions are less shocking than the bone graft procedure, they have their place when chosen for individuals not in physical condition to tolerate the major procedure. The placement of cancellous bone of the neck against the acetabular cartilage, however, is very prone to cause irritation and subsequent arthritis.

The frequency of this pseudo-arthrosis in elderly patients leads one to consider palliative procedures. Will these simpler, less traumatizing osteotomies produce stable, painless hips? The osteotomy of Lorenz aims at placing a portion of the femoral shaft under the head itself, thus passing the weight-bearing stresses directly to the head instead of through the medium of the pseudo-arthrosis (Fig. 8). Schanz described two osteotomies, a high and a low. In this pathological entity, we are concerned only with the high type which is performed in the intertrochanteric region but for the explicit purpose of markedly abducting the distal fragment if the head is movable. When bony union occurs between the femoral shaft fragments in this position and the leg adducted to neutral for weight-bearing, the proximal fragment accompanies the distal which changes the pseudo-arthrosis fracture line from its original vertical position with severe sheering stresses to one more or less horizontal, with associated pressure stresses (Fig. 9). This static change may produce late bony healing of the pseudo-arthrosis as was observed by Schanz and later explained by Pauwels on the basis of Roux's law (13).

Occasionally all operative procedures may fail either because of technical errors or because of shortcomings of the procedures. The final solution is an arthrodesis of the hip joint (Fig. 10). Gill advocates the use of this procedure at an early stage, even 4 months after institution of conservative treatment with failure to obtain bony union. At first glance, this view may be condemned as being too radical but it does decrease the temporary disability and quickly replaces the individual at his occupation, a point of great importance in the laboring class on whom a pseudo-

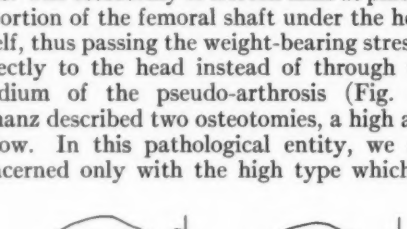

Fig. 6. Magnuson reconstruction.

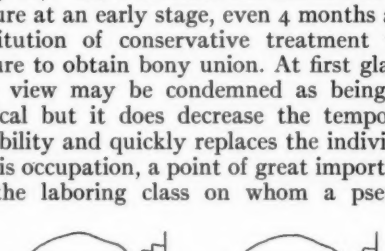

Fig. 7 Brackett reconstruction.

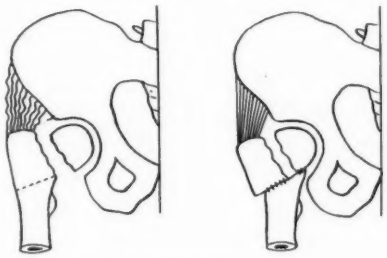

Fig. 8. Lorenz osteotomy.

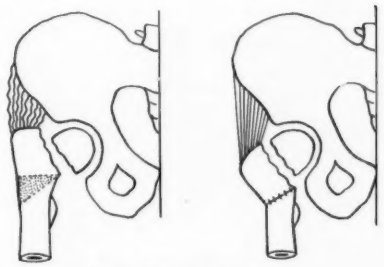

Fig. 9. Schanz osteotomy.

arthrosis of the femoral neck places great financial strain. An arthrodesed hip joint in good position allows the individual to do almost everything easily except lace his shoe; some acquire even this ability. The operative trauma, however, is more severe than that associated with palliative procedures, hence this type of surgery must be reserved for individuals in at least fair general condition.

A large number of patients because of election or poor physical condition must be treated conservatively. In this category falls physiotherapy, crutches, canes, braces, and pelvic belts, or combinations of these. A properly fitted caliper brace with well fitted Thomas ring for ischial weight-bearing relieves the pseudo-arthrosis of sheering stresses. The pelvic belt by its tight compression forces the femora against the ilia, thereby reducing the upward glide of the hip at each step to a minimum. Inductotherm heat has a direct effect on associated arthritic changes.

The following statistics are a composite from the Orthopedic Departments of the Universities of Iowa and Nebraska; division is made according to the type of treatment instituted:

Open reduction with use of Albee bone graft was used in 5 cases—4 males and 1 female, whose average age was 43 years, and who were observed an average of 3.6 years. The results were good with bony union, good motion, no pain in 1 patient; fair with bony union, limited motion, and slight ache in 2 patients; and poor with non-union in 2 patients.

Thus only 60 per cent favorable end-results were obtained. A sixth case seen after having the graft procedure performed elsewhere with a good bony fracture union, had a stiff hip from the extra-articular bone production, doubtless produced by the stripping and dissection necessary for adequate exposure of this area.

Open reduction with use of the Smith-Petersen nail was used in 2 cases, 2 males, 28 and 51 years of age respectively. Average observation was 17 months. One head fragment was necrotic. The results were poor with non-union and increasing varus in both cases. The inefficiency of nailing would seem well illustrated in these 2 cases.

The Whitman reconstruction was done in 18 cases, 5 males, 13 females. The average age was 54 years; average observation, 3.6 years. Three head fragments were necrotic. The results were good with no support needed, useful motion, stable, occasional slight ache in 5 cases; fair with cane necessary, motion slightly limited, occasional slight ache in 4 cases; and poor with crutches necessary, unstable, severe pain or no motion in 9 cases.

The large number of failures, 50 per cent, must be ascribed to the method itself, which

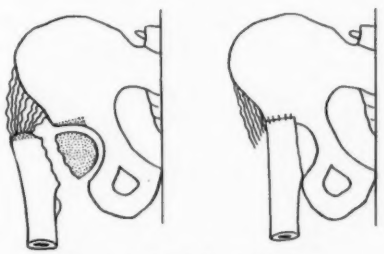

Fig. 10. Arthrodesis of hip joint.

aims at restoration of painless motion with stability. Three of the poor results are due to spontaneous bony ankylosis late after operation which even though serving as stable painless hips must be classified as poor Whitman reconstruction results.

The Brackett reconstruction was used in 3 cases, 1 male, 2 females. The average age of patients was 41.2 years; average observation, 1.2 years. One head fragment was necrotic. The results were good with no support necessary, useful motion, no pain in 1 case; poor with pain or instability in 2 cases.

Of the two poor results, one was due to a technical error, the other to osteoarthritis.

The Lorenz osteotomy was performed in 9 cases, 1 male, 8 females. The average age was 62 years; average observation, 5.4 years. The results were good with no support necessary, motion adequate to tie shoe, slight ache in 2 cases; fair with cane necessary, occasional pain, in 2 cases; and poor with pain marked in 5 cases.

The preponderance of poor results is caused by four technical errors as demonstrated by roentgenograms showing the osteotomy sites either too high or too low or the distal fragments improperly placed under the head; in all fairness to the method, these errors must be excluded which produces 80 per cent favorable end-results.

Schanz osteotomy was done in 3 cases, 2 males, 1 female. The average age was 57 years; average observation 3.3 years. The results were good with no support necessary, no pain, adequate motion in 1 case and fair with no support necessary, occasional slight ache, and restricted motion in 2 cases. Late bony union was not observed.

In 1 case fusion of the hip was done. The patient was a female, age 37 years; observed 3.4 years. The head fragment was living. The result was good.

In the same category may be placed three of the poor Whitman reconstructions which, however, served as good arthrodesed hips. Functionally, these cases had excellent results. The disability connected with an arthrodesed hip joint in 20 degrees of flexion and with neutral abduction and adduction is about 20 to 25 per cent of the entire leg.

The tuber seat brace was used in 13 cases, 6 males, 7 females. The average age was 64 years; average observation 1.5 years. Four head fragments were necrotic. The results were good with no additional support necessary in 3 cases; poor with additional support necessary in 10 cases.

A pelvic belt and physiotherapy were used in 13 cases, 5 males, 8 females. The average age was 66 years; average observation, 1.7 years. Two head fragments were necrotic. The results were good with no additional support necessary in 2 cases and poor with added support necessary in 11 cases.

Twenty-four cases were unsuitable for treatment and of these 7 head fragments were necrotic.

CONCLUSIONS

1. The bone graft procedure of Albee is a radical surgical procedure producing only 60 per cent good results in this series. Its use in individuals of advanced years or with arthritic changes in the hip would seem to be contra-indicated. Certainly the surgeon must be adept and efficient to obtain best results in this procedure.

2. Open reduction and fixation with the Smith-Petersen nail is not adequate for a pseudo-arthrosis with a head fragment markedly atrophic or definitely necrotic. Its use should probably be restricted to treatment of fresh fractures.

3. The Whitman reconstruction which produced 60 per cent favorable end-results is too often followed by late osteo-arthritic changes with associated pain and by instability due to luxation.

4. The Brackett reconstruction, producing 33⅓ per cent good results, is technically more difficult than the Whitman procedure.

5. Both Lorenz and Schanz osteotomies are excellent selections in altering the static stresses about the femoral neck. These procedures are not as severe as any of the reconstructions but offer technical difficulties. Excluding technical errors, end-results were favorable in 87 per cent of cases.

6. Operative fusion of the hip is a radical but sound procedure especially in individuals of the laboring class where quick return to work and stability are essential.

7. As stressed by Brackett, individual case study is necessary in an attempt to determine the procedure the individual will best tolerate and that gives due consideration to his local physical assets, anatomical and physiological. A plan of attack suggested is as follows:

A. If patient's general condition is good with (1) the head living, open reduction, fixation with bone graft should be done; (2) with head necrotic and (a) neck present, reconstruction of Albee or Whitman is method of choice; (b) if neck is absent, reconstruction of Colonna type should be done. (3) If osteo-arthritis is marked, fusion of hip joint is method of choice.

B. If general condition is fair with (1) head living, reconstruction of Brackett or Magnuson type; (2) with head necrotic, osteotomy of Lorenz or Schanz, should be used.

C. If patient's general condition is poor whether head is living or dead the treatment is (a) osteotomy of Lorenz or Schanz or (b) support alone.

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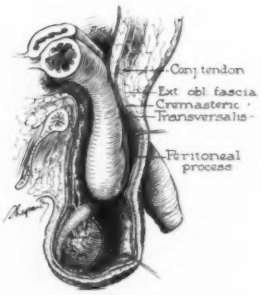

Fig. 1.

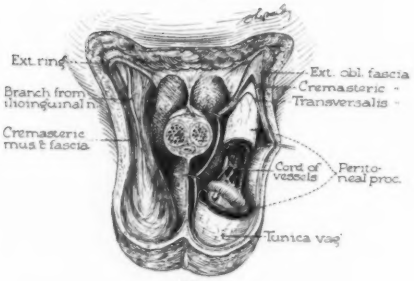

Fig. 2.

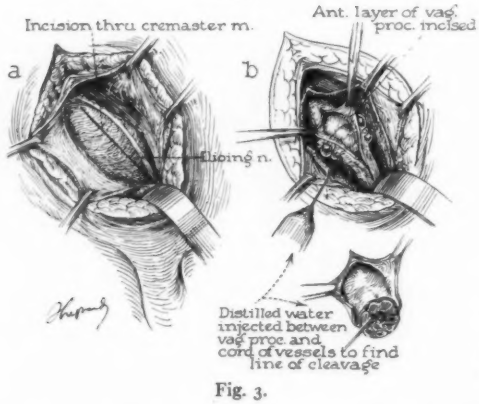
Incision thru cremaster m.
Ant. layer of vag. proc. incised
a
b
Ilioing n.
Distilled water injected between vag. proc. and cord of vessels to find line of cleavage

Fig. 3.

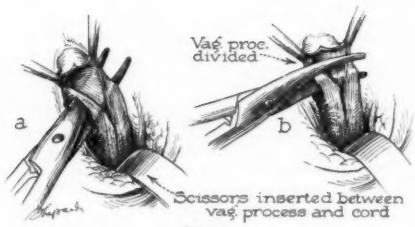

Fig. 4.

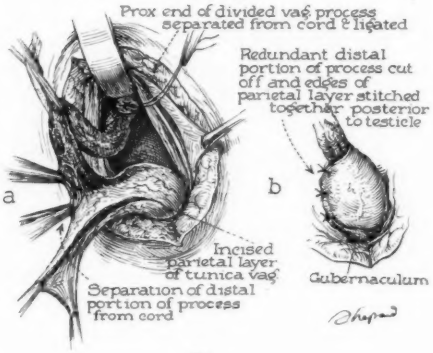
Prox end of divided vag. process separated from cord & ligated
Redundant distal portion of process cut off and edges of parietal layer stitched together posterior to testicle
a
b
Incised parietal layer of tunica vag.
Separation of distal portion of process from cord
Gubernaculum

Fig. 5.

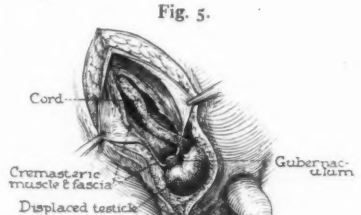

Fig. 6.

Fig. 1. Anatomy of congenital type of hernia into the processus vaginalis.

Fig. 2. The cremaster muscle and fascia is shown covering the lateral and anterior surfaces of the cord and testicle. This structure may completely envelop the testicle. The relationships of the sac in congenital type of hernia are also shown.

Fig. 3. a, Incision through the cremaster muscle in order to expose the cord and peritoneal sac. The fascia of the external oblique has been incised and its leaves retracted. Care should be exercised to avoid the ilio-inguinal nerve. In indirect inguinal types of hernia the peritoneal sac is never found outside the cremaster muscle. b, Injection of fluid between the peritoneal process and the cord in order to facilitate dissection. Either water or normal saline solution may be used. Injection should be done after the sac is opened.

Fig. 4. Method of separation of the sac from the cord by blunt dissection. This may also be accomplished by incision with a knife from the peritoneal side through the injected area.

Fig. 5. a, The proximal end of the divided sac has been separated from the cord and ligated as high as possible. The lower portion is dissected to the level of the epididymis. b, The distal portion of the sac has been everted as in the bottle type of operation. Some surgeons prefer to invert this portion of the sac; others do not disturb it but allow it to drop back unsutured.

Fig. 6. It is essential to replace the testicle within the cremaster muscle. This may be difficult. The testicle is here shown improperly placed outside of the cremaster muscle. The opening in the muscle is not usually as clearly defined as in the drawing.

Technical Notes on Congenital Indirect Inguinal Hernia.—Stanley J. Seeger.

CLINICAL SURGERY

FROM THE MILWAUKEE CHILDREN'S HOSPITAL

TECHNICAL NOTES ON CONGENITAL INDIRECT INGUINAL HERNIA

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THE surgical treatment of congenital inguinal hernia presents several technical problems, two of which deserve discussion. The first of these is the anatomy of the hernial sac and the technique of removing it from the spermatic cord. The second is the anatomical relationships of the cremaster muscle, the hernial sac, the testicle, and the spermatic cord. Failure to observe the importance of these relationships may lead to malposition of the testicle following operation.

The term "congenital hernia" does not refer to the fact that a hernia exists at birth. It describes the type of hernia in which the congenital pouch of peritoneum, which precedes the cord and testicle in its descent, remains patent throughout and unclosed at any point. In congenital hernia the tunica vaginalis communicates directly with the cavity of the peritoneum so that the peritoneal contents may descend within this sac and lie in contact with the testicle. Normally, the processus vaginalis, which is patent for a month after birth in about 50 per cent of infants, soon becomes occluded by adhesion or zygosis at two points. The upper point of occlusion takes place at the internal abdominal ring, and the lower point at a short distance above the testicle. According to Keith, in 30 per cent of children, occlusion takes place at the internal abdominal ring some considerable time after birth or it fails altogether, in which latter case the sac of a true congenital type of inguinal hernia exists. This is in accord with our experience at the Milwaukee Children's Hospital where approximately one-third of the cases of indirect inguinal hernia are of the congenital type.

In dealing with this type of hernia, it is necessary to divide the sac. This is done at approximately the middle. The upper portion is then separated from the spermatic cord and is treated as is the sac in scrotal types of hernia. The lower portion of the sac is variously treated by surgeons. Some surgeons treat the sac as a hydrocele sac; some fashion a new tunica vaginalis; while others do not touch the lower portion of the sac, but allow its divided end to drop back unsutured. The sac is often rather firmly attached to the cord, and in many instances the peritoneum is a very friable structure. Many years ago Bevan suggested that in these cases the dissection of the peritoneum from the cord could be made much easier by the injection of fluid, either water or normal saline solution, between the peritoneum and the struc-

Fig. 7. Inversion of the scrotum over the index finger in order to insure proper replacement of the testicle within the cremaster muscle and fascia.

tures of the cord. This is best done after the sac has been opened, and the posterior layer of the peritoneum, which is adherent to the cord, can be visualized readily. The injection may be made either from the outer side of the sac or from the peritoneal side.

The cremaster is a thin muscular layer which is composed of a number of fasciculi which arise from the middle of the inguinal ligament where these fibers are continuous with those of the internal oblique and also occasionally with the transversalis. These fibers are picked up by the testicle in its descent to the scrotum from the lumbar region. The cremaster muscle passes along the lateral side of the spermatic cord, descends with it through the external inguinal ring, lies upon the front and sides of the cord, and forms a series of loops which are united by areolar tissue. This thin covering over the cord and testicle is the cremasteric fascia. At times it completely surrounds the testicle and cord. The fibers are inserted by a small pointed tendon into the tubercle and crest of the pubic bone and into the front of the sheath to the rectus abdominis. Ogilvie has recently commented on the physiology of the cremaster muscle stating that this structure is "the most maltreated by surgeons." In indirect forms of inguinal hernia the sac is never found outside the cremaster muscle and fascia. In congenital types, if one treats the lower half of the sac as a hydrocele or fashions a new tunica vaginalis, it is necessary to deliver the testicle through the opening which has been made in the cremaster muscle.

After the sac has been treated either by eversion, as in the bottle type of operation for hernia, or by inversion, and the formation of a small vaginal process, one may find that it is difficult to replace the testicle within the cremaster. Forceful efforts to replace the testicle within the scrotum may result in its placement outside the cremaster muscle. This technical error will lead to subsequent malposition of the testicle, usually on the pubic bone, with consequent discomfort. Should the opening in the cremaster not be located readily, or difficulty of any kind be experienced in replacing the testicle within the scrotum, the proper channel can be found easily by inverting the scrotum over the tip of the finger. This maneuver obviates the possibility of error. At the conclusion of the operative procedure the scrotum should again be examined to make sure that the testicles are in their normal position.

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FROM THE SURGICAL UNIT OF THE WELSH NATIONAL SCHOOL OF MEDICINE, CARDIFF

THE TREATMENT OF THORACIC EMPYEMA

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THE technical details of empyema drainage are simple: the chief responsibilities of the surgeon are to determine when, where, and for how long to drain. If the chest is opened too soon especially for synpneumonic empyema the vital capacity already decreased will be further lowered by severe mechanical disturbances of the mediastinum which follow the creation of an open pneumothorax before the abscess has localized or the central structures have become fixed by adhesions. Brock[1] has also demonstrated that the entry of air to the pleural cavity encourages absorption of pleural fluids: if the effusion is purulent, the toxemia is thereby increased. Sudden decompression by the withdrawal of large quantities of fluid may cause death. If, however, drainage is postponed too long, thickening of the visceral pleura and prolonged collapse of the lung will delay that expansion of the lung which is so necessary for obliteration of the empyema cavity. The correct moment for drainage is when the pus is moderately thick. Acute empyema in infants causes a fairly high mortality rate partly because of the extreme mobility of the diaphragm and because of too early drainage by open operation.

PREPARATION

Pleural puncture and aspiration. Since empyema is never an acute surgical emergency, the pre-operative management can be carried out deliberately. Our first duty is to ascertain the type of pleural exudate and its bacteriology by paracentesis. A common error is to allow air into the chest during the aspiration of the fluid (whether done for diagnostic or therapeutic reasons) and this is due to slovenly technique.

METHOD

Diagnostic puncture. If the empyema is basal the patient is propped up and leans forward on pillows or a cardiac bed rest. In nervous subjects a sedative is employed and no hesitation is felt about using morphia in reasonable doses. The skin overlying the intercostal space is infiltrated with 1 per cent novocain and then the deeper tissues including the parietal pleura through the hypodermic needle mounted on a 2 cubic centimeter record syringe. After full anesthetization the same needle is advanced into the pleural cavity. If the purulent fluid is thin it will be drawn easily through the hypodermic needle. If no fluid is obtained the pus is probably thick and a larger needle on a syringe is employed and a sample of pus is withdrawn and examined bacteriologically. Under no circumstances is the barrel of the syringe disconnected while the needle is in the pleural cavity, as air would thereby enter.

Therapeutic aspirations. These are performed under local anesthesia: in this clinic a two way syringe of the Dieulafoy type (Fig. 1) is preferred to a Potain aspirator or a reversed artificial pneumothorax apparatus. The apparatus is assembled as shown in Figure 1, and the needle introduced into the pleural cavity. The plunger is withdrawn until the barrel of the syringe is full and then the two way tap is turned and the pus is expressed into a receiver. The maneuver is repeated until sufficient pus has been removed. The onset of cough or dyspnea is an indication to cease aspiration.

The disadvantages of repeated aspiration. In nervous patients repeated skin anesthetizations are undesirable and the needle tracks may get infected. The simple operation advised by Tudor Edwards is extremely valuable in such conditions. Under local anesthesia a segment of rib is resected subperiosteally and the wound is lightly packed with flavine gauze. When aspiration is required the gauze is removed and the pus is evacuated by a two way syringe: the procedure is quite painless. After an interval the pus becomes thicker and then the pleura is incised and continuous tube drainage is instituted.

INTERCOSTAL DRAINAGE

Repeated aspiration of thin streptococcal effusion in ill patients may be too disturbing or fail to control the toxemia and the pressure disturbances, and closed air-tight intercostal drainage is then desirable. This is usually accomplished

[1] Brock, R. C. Observations on pleural absorption. Brit. J. Surg., 1933–34, 21: 650.

Fig. 1. Two way syringe used for therapeutic paracentesis. The trocar is shown partly withdrawn.

by passing a trocar and cannula through an anesthetized area into the pleural cavity: the trocar is then withdrawn and a self retaining catheter of the de Pezzer or Malecot type is inserted by means of the appropriate introducer. In this clinic the following simple maneuver has proved useful and efficient:

Preliminary treatment. The patient need not be moved to the operating theater. A preliminary sedative such as morphia is given and the chest wall is sterilized in the usual manner. The patient leans forward on pillows or a cardiac rest.

Apparatus required. (1) *The trocar.* The one employed is that designed by Hamilton Bailey for use in performing suprapubic cystostomy[1] (Fig. 2). (2) *The catheter.* This is of the Malecot type and has a specially re-inforced tip (Fig. 2). (3) *The drainage bottle.* The whole apparatus is assembled as shown in Figure 3. The sterilized catheter is connected by a hollow glass tube to a length of rubber tubing which is attached to a long glass tube leading through a perforated rubber bung to antiseptic fluid in the bottom of the bottle. This is to ensure a water sealed drainage system; a smaller glass tube allows air and gas to escape from the system.

The operation. The overlying skin and pleura are thoroughly anesthetized with novocain 1 per cent solution. After the pleura has been infiltrated the needle is advanced through it still connected to the barrel of the syringe. The plunger is then withdrawn and the escape of pus will confirm the choice of site for drainage. A small incision is made through the skin. The trocar is passed through the tip of the catheter which has been assembled to the drainage bottle in order to prevent the entrance of air into the chest at any stage of the operation. The

[1]This trocar and the catheter used with it are made by the Genito-Urinary Manufacturing Co., London. W. I.

Fig. 2.

Fig. 2. Hamilton Bailey's suprapubic cystostomy trocar and Malecot's catheter (above).

Fig. 3. Trocar, catheter, and bottle assembled and ready for use in performing intercostal drainage.

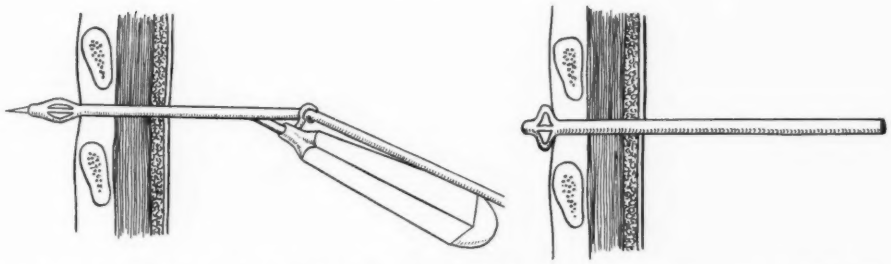

Fig. 4. a, left. The trocar and catheter after the parietal pleura has been punctured. b, After withdrawal of the trocar.

catheter is stretched out along the trocar to flatten out the flange. (The metal cuff at the base of the bayonet point will prevent the trocar from perforating the catheter tip too far). The trocar is pushed into the pleural effusion until the flange is past the parietal pleura. The catheter is then allowed to relax so that the rubber flange opens out and is left fitting snugly against the parietal pleura when the trocar has been withdrawn (Fig. 4). Pus can now flow out of the chest without loss of the negative intrapleural pressure. This will be demonstrated by observing the rise and fall of the fluid in the long glass tube with each respiratory excursion. This method is not to be used as a substitute for formal rib resection and drainage except occasionally in children. Its main employment is as a preliminary to rib resection and in the management of secondarily infected tuberculous effusions.

Disadvantages of intercostal drainage. The tube may become blocked by fibrin clots and will easily slip out of the chest unless fixed to the skin by a silkworm gut suture. If the pus ceases to flow out, the tube should be "milked"; if this fails the patency of the tube should be tested by passing a gum elastic bougie or a metal stylet along it. Repeated blockage by fibrin clots indicates the necessity for rib resection and drainage.

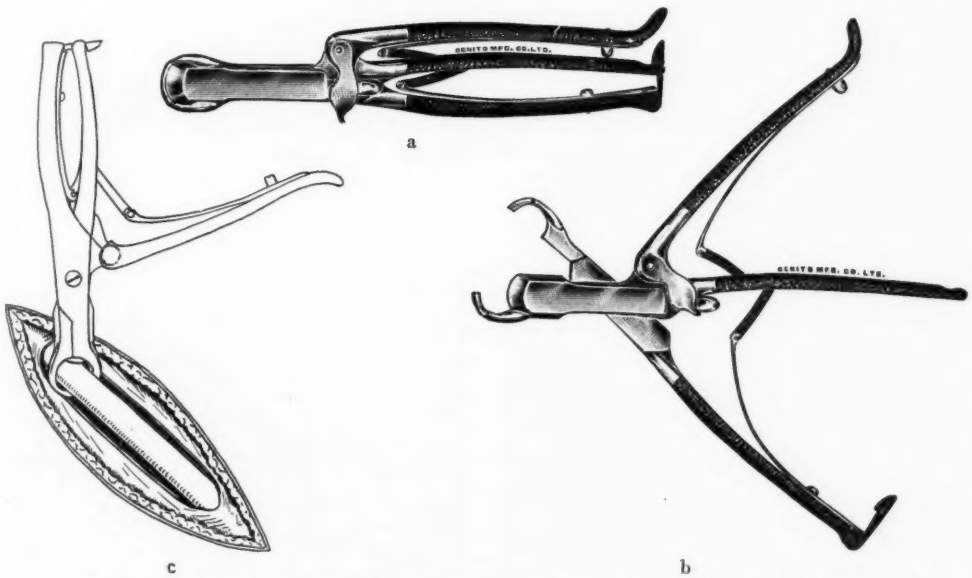

Fig. 5. a and b. Tudor Edwards' costotome. c, The costotome in position and about to divide the rib.

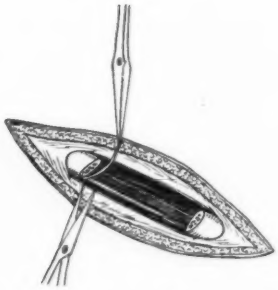

Fig. 6. Excision of segment of intercostal nerve after rib resection to prevent postoperative pain.

RIB RESECTION AND PLEUROTOMY

The advantages and disadvantages of closed and open drainage will be discussed later. When the pus is creamy no time should be lost in carrying out rib resection and pleurotomy. The patient is preferably placed lying on the sound side with the front of the thorax supported by a chest piece padded with sorbo rubber or supported by pillows and sandbags: the head and upper part of the thorax are well raised by pillows. The operation is usually carried out under local anesthesia: in very nervous patients or young children, gas and oxygen is administered.

Site for resection. The site for resection depends entirely on the situation and size of the empyema. In basal empyema the commonest site is just above the lowest level of the cavity in the midaxillary line. If the tube be placed too low the ascent of the diaphragm (which usually follows drainage) will block the tube. The ninth rib is certainly the lowest that should be chosen and usually better results follow removal of portions of the seventh or eighth ribs. If the opening is further forward than the midaxillary line the pus will gravitate further backward and escape evacuation: if the tube is too posterior, the position of the patient as he lies in bed will block the tube if (as is usually the case) closed drainage methods are employed. Moreover the investigation of chronic empyema sinuses shows that the posterolateral part of the lung is usually later in expanding than that occupying the costovertebral sulcus. Apical empyema cavities are drained anteriorly or in the axilla, while interlobar empyema cavities are drained according to their anatomical location by anteroposterior, lateral, and oblique roentgenological views.

The incision. An incision (about 2½ inches) that is oblique rather than along the line of the rib is preferred for the following reasons: (1) The muscle fibers can be split along the direction of their fibers, and this prevents the tendency for cellulitis or suppuration to proceed along muscular planes, and (2) the tube lies more comfortably since in an incision along the line of the rib the skin opening frequently does not correspond accurately with the opening made in the pleura after rib resection.

Before the periosteum over the rib is incised the empyema is needled to confirm the presence of pus directly beneath the space to be opened. If the needling shows that an error in choice of rib has been made, an oblique incision can readily be enlarged either up or down, and another space needled. The periosteum of the rib is incised for 2 to 3 inches and then cleared by a Faraboeuf's raspatory. It is unnecessary to emphasize the well known rule that when the periosteum is cleared from the ribs the operator should work along the line of the intercostal muscles, i.e., in clearing the upper edge the raspatory passes from behind forward and in reverse direction when clearing the lower edge. A Doyen's raspatory clears the periosteum from the deep surface of the rib. Two inches of rib are then removed by means of bone cutting forceps or better, by using a costotome of the Vermehren type (that illustrated is devised by Tudor Edwards, Fig. 5).

The intercostal nerve. A common complaint by the patient after rib resection and drainage is pain which radiates anteriorly along the course of the intercostal nerve and this is due to the pressure of the tube. To prevent this the nerve is exposed by blunt dissection of the neurovascular bundle after the rib has been resected. A suitable portion is then excised (Fig. 6). We have found this little addition to the operation to be of great benefit.

PLEUROTOMY

The posterior periosteum and the pleura are incised and the cavity is explored with the finger to make sure that the tube will lie near the bottom of the cavity. In pneumococcal postpneumonic empyema large fibrin clots may require removal with forceps as otherwise they will block the drainage tube. Unless the pus is exceptionally thick, closed drainage is always employed. The reasons for this are: (1) that it enables a negative pressure to be established in the thorax and this greatly aids the rate of pulmonary expansion; (2) that it does away with the necessity for frequent and disturbing changes of dressings; and (3) it allows the cavity to be irrigated without disturbing the patient appreciably. The Tudor

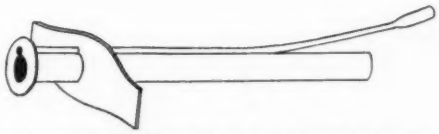

Fig. 7. Tudor Edwards' tube for closed drainage.

Edwards' type of tube is used (Fig. 7) and the muscles are sutured around this to ensure air tight drainage and to anchor it firmly. After the wound has been lightly closed with interrupted silkworm gut sutures, the outer flange of the tube is fixed in place with elastoplast strips (Fig. 8) and connected to a bottle, as after intercostal drainage, and a clip is placed on the small irrigation tube.

Postoperative care. The patient is propped up in bed immediately on returning to the ward and from the outset is encouraged to breathe deeply. Great assistance in this respect is obtained by the use of breathing exercises conducted twice daily under the care of a masseuse. As soon as possible the patient is encouraged to drink and eat normal food to remove the atmosphere of invalidism. On the next day the empyema is washed out with Dakin's solution. This irrigation prevents the tube from being blocked and is a powerful dissolver of fibrin and so prevents a thick deposit of fibrous tissue developing over the visceral pleura which might delay lung expansion. If there is a bronchopleural fistula, irrigation is not employed; such a complication is detected at once if the patient says that he can taste the fluid or if he coughs violently as soon as the irrigation is commenced. If the tube becomes blocked a stiff gum elastic bougie is passed down the rubber tube; if this together with irrigation fails to produce a clean passage the tube is taken out and the wound is searched for fibrin clots which are removed and the tube is re-inserted.

When to remove the tube. The cavity requires a drainage tube until the lung has completely expanded out to the chest wall. The commonest cause of a chronic empyema is premature removal of the tube. If the closed drainage system is working adequately and pus is escaping, the system can be maintained for weeks or months. The safest method of estimating lung expansion is by means of a roentgenogram taken after lipiodol has been allowed to run into the tube with the patient lying on his sound side. By this means the exact boundaries of the cavity can be delineated and faulty positions of the tube noted and corrected. (The tube may require lengthening or shortening.) In many patients the closed

Fig. 8. Closed drainage system.

drainage system can be dispensed with in about a fortnight, and an open tube substituted and the pus allowed to flow out on to the dressings. The advantage of such a conversion is that the patient can be allowed to get out of bed. If, however, the lung is slow to expand, a continued use of the closed drainage together with the application of suction drainage is indicated. Even with cases of long standing chronic empyema (the treatment of which cannot be described here) re-drainage by this method may be so effective that thoracoplasty and other measures can be avoided.

PROGNOSIS

In previously healthy adults the prognosis of acute empyema is very good provided the cause of the empyema is a straightforward pneumonia and not a result of generalized septicemia and pyemia. Empyema secondary to bronchiectasis and lung abscess is a grave complication and is often a terminal event in carcinoma of the lung or esophagus. From time to time empyema may be the outstanding feature in bronchial obstruction due to innocent or malignant tumors of the bronchus, and the investigation of chronic empyema fistulas should include the appropriate investigation of such causes (bronchoscopy, lipiodol bronchography). Occasionally a patient is referred with a diagnosis of empyema when the true condition present is that of suppurating congenital cyst of the lung. Empyema is a serious condition in infants under the age of two and in elderly patients. Though possessing peculiar risks of its own, bilateral empyema can frequently be managed with complete success, each side being treated strictly on its own merits, open drainage being used only when the pus is thick.

CONSERVATIVE MYOMECTOMY

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IN the gynecological literature the question is discussed again and again as to whether, in operating on a myoma, supravaginal amputation of the uterus or total extirpation should be performed. This question, however, should be considered only in women past the menopause; in the childbearing period total extirpation should not enter into the discussion. The surgeon is obliged to carry out his operations in as conservative a manner as possible in order to maintain menstruation in the woman.

For a considerable time operative gynecology was ruled by the assumption that menstruation is an unphysiological process. As long as we placed the ovum in the center of the generative processes, menstruation—as the expression of the death of the ovum—was considered as an unimportant and unphysiological occurrence. Experimental investigations (3, 4, 6), however, demonstrate that the ovum in itself has no importance in the hormonal regulation of the ovarian functions, that the ripening of the follicle and the production of folliculin, luteinization and progesterone production are independent of the ovum. The function of propagation is dominated by the anterior pituitary, for without the anterior pituitary and without the gonadotropic hormone the ripening and the rupture of the follicle is not possible. Without the anterior pituitary the ovum would never unite with the spermatozoon. It is not the ovum but the anterior pituitary that dominates the whole generative process; it governs the follicle with its enclosed ovum as well as the ovarian hormones (estrone and progesterone) produced secondarily in the follicular cells. The task of the ovum during its presence in the ovary is exclusively that of preparation for fertilization. The ovum, however, does not participate in the constructive process of the uterine mucosa necessary for its nidation. This latter is brought about by the ovary under the influence of the anterior pituitary.

Based upon this biological knowledge we can no longer consider menstruation, as did Robert Meyer, in a certain respect as a pathological process, but, on the contrary, as a process specifically intended by nature for the case when the ovum is not fertilized. In most of the mammals the generative cycle occurs without bleeding. It cannot be accidental, or unintentional, that in primates this process is accompanied by bleeding. Although hitherto we have been unable to explain the meaning of menstruation in a physiological sense, we must not conclude, however, that our insufficient knowledge should compel us to disregard the importance of menstruation. There is one property of the menstrual blood which distinguishes it in a characteristic manner from the remaining corporal blood, that is its incapability to coagulate. If we consider menstruation as a pathological process not intended by nature it is incomprehensible why menstrual blood should have other properties than the corporal blood. The concentration of follicular hormone in the menstrual blood is seven times as high as it is in the blood of the general circulation (R. T. Frank and Goldberger). Menstrual blood, therefore, participates in the excretion of folliculin which has not been used by the organism. Menstrual blood does not coagulate for otherwise it would form a large clot in the corpus uteri and would impede the cleansing of the uterus, i.e., the discharge of the uterine mucosa during menstruation. If, therefore, menstrual blood demonstrates its purpose by its inability to coagulate, the discharge of the blood in itself, i.e. menstruation, must have a physiological importance. Menstruation is not a passive but an active process induced by special hormonal action, probably by a hemorrhagic substance (5). The discharge of menstrual blood has, in addition, as every physician knows, a very great psychic importance. These facts should teach gynecologists to proceed as conservatively as possible in operative manipulations in order to maintain wherever possible the menstrual hemorrhage in women of a sexually mature age.

There should be no discussion of the question as to whether in operating upon a myoma the uterus should be amputated supravaginally or totally extirpated. The supravaginal amputation should be preferred and performed as high as possible in order to preserve a part of the uterine mucosa from which menstruation may take place. If, however, for technical reasons (if, for example, the whole uterine wall is involved

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by the myoma), the supravaginal amputation cannot be performed, the uterine mucosa should be implanted in the cervix following the low supravaginal amputation in order to give the uterus the possibility of menstruating. Even in women near or beyond the menopause supravaginal amputation is advisable because in this manner the configuration of the vagina is better preserved and difficulties in coitus are eliminated, a fact to which the surgeons pay far too little attention. In addition, the supravaginal amputation is a simpler and safer operation for the patient than total extirpation.

In the literature, one of the reasons often given for performing total extirpation in young women is the opinion that if a stump remains, a collum carcinoma can occur. This fear seems to me to be greatly exaggerated. I understand, indeed, that in older women this viewpoint can be considered. I do not understand, however, why in young women, for prophylactic reasons only, menstruation should be disturbed as well as the configuration of the vagina. It would not occur to any surgeon to extirpate the mamma in a woman who suffers from a fibroma of the mamma, because later on she might develop a carcinoma.

In my former work in Germany I believed in the conservative point of view regarding the operation on myoma but during my practice in Palestine I have gone still further, owing to the impressions which I have gained here. The desire for a child is so strong among the women of Palestine, the preservation of the uterus plays such an important rôle, that the women prefer to undergo the greater danger of the conservative myomectomy if there is the slightest possibility of preserving conception. If in my former practice I told the women that after myomectomy I should endeavor to preserve menstruation they were for the most part satisfied. But in this country the women agree to this solution only if they have already had several children. This attitude is due particularly to the natural feeling toward children, perhaps, however, to the fact that a childless marriage of 10 years' duration is legal ground for divorce. Under this impression, I have adopted a more conservative method of operation. I have seen that even in the presence of monstrous tumors, even if the uterus is permeated by tumors or if the tumors are situated antecervically or retrocervically, intraligamentarily or submucously, the conservative operation can be used. Nor degenerative changes of the myoma contra-indicate the use of the conservative method. While the conservative method is a well known procedure, it is used only in exceptional cases.

In this paper I shall discuss my experiences since I have been using the conservative operative method, although in this country the number of difficult cases is very large.

In Jerusalem I have performed, up to the present time, 82 myoma operations, 40 of which were conservative, or 48.8 per cent.[1] The conservative myoma operation, of course, is justified only in women of a sexually mature age, i.e., up to an age of about 40 years. In this age group I have operated upon 67 women, and of this number conservative operation has been performed in 40 cases, that is in 59.7 per cent. Thus I have succeeded in preserving the uterus and both of the ovaries, or at least one, in more than half of the cases, so that the women not only menstruated but, in addition, possessed the possibility of conception. The percentage (59.7) includes the operations during my first year here as well, when I had not begun to use the conservative operative method so freely as I have done since. I have gradually increased the indications for this operation. Conservative myomectomy should not be performed if the woman is in the middle or at the end of the third decade and has already had children. In such cases it is sufficient to maintain menstruation. Of 67 women of a sexually mature age in 10 cases it was unnecessary to do the conservative operation as they had already had children. Therefore, the conservative operation was indicated in 57 cases and of this number 40 patients were operated on by the conservative method, that is in 70.2 per cent. Of my last 10 cases, 9 were operated upon by the conservative method.

The technique of the conservative operation is, no doubt, much more difficult than that of the supravaginal amputation or total extirpation. All these operations require typical methods, but conservative myomectomy is atypical; once the abdominal cavity is opened, a plan must be made according to the case. It is not sufficient to remove the myomas but in addition it is important to spare the musculature as far as possible in order to preserve a uterus capable of its function in pregnancy and parturition. If the uterus, following the operation, is a slack, weak organ it is, indeed, capable of menstruation but incapable of carrying the child and functionating in parturition. In such cases the high supravaginal amputation is the better way. The important points in the conservative operation are the following: (1) Every myoma must be enucleated; (2) the orifices of both tubes or, at least, of one of them must be spared; (3) the uterus must be recon-

[1] In the meantime 8 more patients have been operated upon according to this method, so that there is now a total of 48 cases.

structed in such a manner as to preserve as much of the muscular tissue as possible. In order to test the last point, I inject during or at the end of the operation one ampoule of posterior pituitary extract (pitocin) into the reconstructed uterus. The reaction to this injection becomes apparent by the contraction and rigidity of the uterus and thus, according to the degree of contraction, the presence or absence of sufficient uterine musculature is demonstrated.

If the myoma is situated antecervically, the bladder must be dissected off for a great extent; in case it is situated retrocervically and adheres to the rectum, the latter must be sharply dissected away. If its site is within the ligament, the ureter must be dissected off. If the omentum or the small intestine adhere to the tumor they must be separated. I have learned from the literature that there are surgeons who, after having ligated the uterine artery on one side, decide to perform amputation of the uterus fearing a deficient circulation in the uterus, with consequent nutritional disturbances. This view is faulty. As a matter of fact, it is possible to ligate the uterine artery on one side without any disturbance occurring. Conservative myomectomy, no doubt, gives occasion for infection in a much higher degree than the radical operation because of the large wound cavities. Extreme attention must be paid, therefore, to asepsis during the operation.

I use the transverse abdominal incision at the level of the border of the pubic hair, or somewhat higher, so that later the incision is scarcely noticeable. This incision has the advantage that no postoperative hernias occur and the patient is not obliged to wear any kind of support whatsoever. In addition, the low transverse incision is much better cosmetically than the median incision. The size of the tumor is not a contra-indication to this type of incision. Even tumors which reach up to the costal arch can be removed through a transverse abdominal incision.

The use of a continuous intravenous drip of normal saline or a 5 per cent glucose solution has proved to be very practical if given before the operation takes place. This step is most effective in avoiding or combating postoperative shock and peripheral circulatory disturbances.

In the group of conservative operations I found degenerated tumors in 9 cases. Frequently there were different sorts of degeneration in the same case, namely: hyaline degeneration, cystic softening (twice), beefy color, hemorrhages into the myoma (twice), thrombosis, and beginning necrosis of the myoma (7 times). Formerly I believed that such patients should not and could not be operated upon conservatively. Experience, however, has taught me that myomas with hyaline degeneration, with cystic softening, tumors with hemorrhages and even with beginning necrosis, can be removed with conservative measures. The question becomes difficult to decide when there is a thrombosis in the myoma. Each case must be judged separately. Every nodule of the myoma must be inspected by transverse section during operation in order to avoid the danger of overlooking the presence of malignant degeneration. Every suspicious portion must be examined by the pathologist during operation, both macroscopically and microscopically. This examination can generally be performed in a few minutes. The bed of the myoma must be very carefully sutured in three layers to eliminate wound cavities. At the end of the operation the uterus must be absolutely dry.

The course after a conservative operation frequently is not so smooth as that after a supravaginal amputation. During the first 2 days after operation the temperature is usually above 38 degrees C. then it usually becomes lower and remains subfebrile for a few days. I keep the patients in bed for 2 to 3 weeks after conservative operations.

All our results have been good except for one fatality. Forty-six hours after operation, the pulse was normal, and the abdomen soft. In the evening at 9 o'clock she spoke to the nurse, and 20 minutes later she was found dead in bed. Autopsy revealed a pulmonary embolism.

CASE REPORTS

Since it is impossible to report all the cases in detail I shall give the operative records of only a few cases in order to demonstrate the value of the conservative operative method.

CASE 1. A., aged 30 years, had been married for 6 months. Menstruation had been regular and had lasted 7 days, with marked blood loss. The patient suffered during her menses from severe pain in the back and abdomen.

Operation was performed May 1, 1936, with chlorethyl ether-narcosis. The transverse abdominal incision was used. The tumor extended a hand's breadth above the umbilicus, corresponded in size to an 8 month pregnancy; it was so wide that it filled the whole abdominal cavity. So many tumors were present that the uterus itself could not be recognized. It was only with difficulty that we succeeded in elevating the tumor outside the abdominal wall. We then saw that the tubes were so adherent to the fundus of the tumor that, at first glance, the conservative operation appeared to be impossible. However, since the preservation of the uterus was of extreme importance in this patient we tried the conservative method, realizing, however, that at the end of operation amputation could still be performed. The uterus was covered with subserous

tumors. On the fundus there was one tumor the size of a child's head, and a second the size of a fist. On the anterior wall there were 12 tumors varying in size from that of a cherry to an orange. On the posterior wall there were 8 tumors, laterally both on the right and left there were several tumors varying in size from that of a cherry to a plum. After the tumors of the fundus had been enucleated we gained access to the uterus itself. In this case we first divided the uterus sagittally in order to ascertain whether there were tumors in the muscular wall; whether there were submucous tumors in the uterine cavity, and whether after removal of the tumors sufficient muscular tissue remained to permit us to reconstruct a uterus capable of functioning. The circle of tumors surrounding the sagittal section on the anterior and posterior wall was excised together with a piece of musculature. A small tumor of mandarine-size situated directly at the tubal orifice, was divided and very carefully shelled out of its bed. The tube could be easily shifted, so that the junction of the orifice with the uterine cavity was well preserved. At the same time from the sagittal section some intramural nodules were removed. In the remaining portions of the uterus intramural nodules could not be observed macroscopically. On the posterior wall a tumor protruded into the uterine cavity so that we had to open the cavity through an incision 1.5 centimeters in diameter. The cavity was then closed with several sutures. Removal of the lateral tumors was technically difficult. After the broad ligament was divided, the tumors could be excised without, however, the ureter appearing. On transverse section two of the tumors showed degenerative changes, namely hemorrhages and softening. The histological examination performed during operation excluded malignant changes. The beds of the myomas were sutured in three layers so that no gaps occurred in the tissues. After injection of 1 cubic centimeter pitocin the uterus contracted excellently and was the size of a normal uterus. Both tubes were patent. The orifices of the fallopian tubes had certainly not been injured. Finally the uterus was wrapped around with omentum. The patient thus kept her uterus and remained capable of conception. A total of thirty tumors had been removed. The follow up examination several months later revealed that menstruation was normal in every respect. The uterus had a normal configuration and sounding showed a length of 6.5 centimeters.

CASE 2. H., aged 28 years, married 10 weeks. The menstruation had been regular and had lasted 3 to 4 days; on the second day the loss of blood had been remarkable. For the past 2 years, particularly, the patient had observed that the circumference of her abdomen had increased considerably. She suffered from constipation.

The uterus was pushed to the right by an enormous tumor filling the entire abdomen. The upper edge of the tumor was two finger breadths beneath the costal arch, and the tumor filled the left parametrium and Douglas' pouch.

Operation was performed on June 16, 1936, with chlorethyl-ether-narcosis and through a transverse abdominal incision. After the peritoneum had been opened an enormous tumor reaching almost to the costal arch appeared. At first it could not be determined whether this mass consisted of a cyst, a pregnancy, or a myoma. Examination of the tumor revealed that it was a very large softened myoma. On the left the tumor adhered to the cervix and extended to the wall of the pelvis between the layers of the broad ligament. The uterus itself was covered with five subserous tumors varying in size from a cherry to a mandarine. Difficulty in removing the left-sided tumor was encountered in the lateral areas where the tumor reached the ureter and the uterine artery. This section was loosened at first by separation of the broad ligament, dissecting off the ureter and freeing the tumor laterally from the large blood vessels. The left uterine artery was ligated. After one side of the tumor had been freed, the retrocervical portion was dissected away. Now the uterus with its immense tumor and small subserous myoma was freely movable. We did not meet with any technical difficulty in extirpation and enucleation of the other tumors. The uterus was precisely sutured in three layers and the result was a normally shaped uterus. Both tubes were patent and we were sure that they communicated with the uterine cavity. The ovaries were normal. Finally the uterus was wrapped around with omentum. Thus the patient had preserved a uterus capable of conception.

CASE 3. F., aged 36 years. Menstruation was regular and lasted 8 days. The loss of blood was considerable. During the latter years the patient constantly suffered from pain in the abdomen so that she was severely incapacitated in her work. She had been married for 9 years and had been anxiously longing for a child. This was the patient mentioned above who afterward died from a pulmonary embolism. The tumor extended a hand's breadth above the umbilicus, corresponding in its size to a pregnancy of the seventh or eighth month. It filled the whole hypogastric region and Douglas' pouch so as to push the uterus forward against the symphysis.

Operation was done May 5, 1936, with transverse abdominal incision. After having opened the abdominal cavity we saw a monstrous tumor consisting of a large number of single nodules. One tumor the size of a man's head was situated retrocervically and filled Douglas' pouch like a mold. The uterus which was pushed forward showed at the fundus and on the anterior wall a circle of smaller myomas varying in size from a cherry to a plum. Furthermore, there was a tumor the size of a child's head in the intraligamentary region, on the right. The tumor was so firmly fixed by means of this last tumor and by the tumor in Douglas' pouch, that it could not be moved in any way. In order to elevate the tumor from the pelvis we had at first to excise the intraligamentary nodule on the right. In order to approach the latter the broad ligament on the right was divided. The intraligamentary tumor could now be grasped by forceps. After having dissected off the ureter the tumor was divided and was shelled out without difficulty. We were then able to reach the tumor in Douglas' pouch, which was divided sagittally and removed in two parts. The posterior wall of this tumor was adherent to the rectum over a broad area of about 10 centimeters in diameter. The rectum had to be dissected away from the tumor with small forceps and scissors. After the tumor in Douglas' pouch had been removed, there was no further difficulty in the operation. There were more than 20 smaller nodules which were enucleated and sutured one by one. Since the tumors lay close together near the midline some of them were closed, in three layers, by means of the same suture. At the fundus three tumors of mandarine-size were enucleated. We had to remove a total of 30 tumors. On the first and second day after operation the condition of the patient was exceedingly good. The abdomen was soft, the pulse good. Flatus had escaped and the stools were discharged. Spontaneous urination was possible. Forty-six hours after operation sudden exitus occurred because of pulmonary embolism.

CASE 4. The patient was 35 years old. Menstruation used to last for many days and was accompanied by a considerable loss of blood. She had been married for 2 years. She had had one abortion and was anxiously longing for a child. The transverse abdominal incision was used.

TABLE I.—PREGNANCY AFTER CONSERVATIVE MYOMECTOMY

Name Age	Number of years of marriage	Deliveries before	Abortions before
R. 30	6	None	None
B. 28	5	None	None
K. 30	6	None	None
S. 30	11	None	1
G. 32	11	None	1
Sch. 30	6	None	3
W. 32	5	None	1 premature delivery 3 abortions

At first the appearance of the uterus seemed normal showing only some small subserous nodules on the posterior wall. The main tumor could be found only by palpation. It filled the depth of the pelvis so that the cervix itself was not palpable. It was, therefore, a myoma of the cervical portion.

After the bladder was dissected away from the tumor the latter was drawn forward with forceps, divided sagittally, and then loosened from the cervix. On this occasion we saw that the tumor originated exclusively from the anterior wall of the cervix. The left uterine artery had to be ligated. The large wound bed was sutured in two layers. This case demonstrates that in a large antecervical myoma the conservative operative method can be used.

TUBAL FUNCTION

The conservative operative method attains its purpose only if the capability of conception can be restored. This is not possible in every case and if this becomes apparent during the operation there is no further purpose in proceeding conservatively. In the majority of cases, at least one of the orifices of the fallopian tubes, can be preserved. If one has to enucleate a tumor near the tube one should take special care not to open the lumen. I divide the myoma sagittally and dissect out every part separately from its bed. In this manner we are most likely to preserve the tubes.

The preservation of the tubes, therefore, is the most important factor during the operation. Only by a subsequent hysterosalpingography can we see whether the operation has been successful in regard to this point. I have had the opportunity of examining only 4 cases subsequent to operation. In 3 of them the tubes were patent on both sides or at least on one side. In one case the tubes could not be depicted. This event, however, does not prove that the passage of the tubes is not free. Every one who is experienced in salpingography knows that an impeded passage is not proved if the tube cannot be depicted, since the entrance of the lipiodol into the tube can be prevented by spasms as well. We were particularly careful with the roentgenological proceeding after conservative operation in order to avoid too great a strain on the uterine musculature. In many of our cases the follow-up examination was not necessary since the situation of the tumors excluded any possibility of injury to the tubes. In addition, as we shall see later, in some of the cases pregnancy occurred, whereby the intactness of the tubes was best proved. The pregnancies occurred even before we had decided to perform salpingography.

PREGNANCY AFTER THE CONSERVATIVE OPERATION

Up to the present, 7 women have become pregnant after the conservative operation.[1] Pregnancy as well as parturition and puerperium have been normal. All these women had been married for several years and were childless. There is no doubt that it was only by operation that the sterility or the habitual abortion had been corrected (Table I).

Table I shows that pregnancy after conservative myomectomy occurred in young women 28 to 32 years of age who had been married from 2 to 11 years without having had children. In 3 of the women there had never been a pregnancy, 4 of the women had suffered from one to three abortions. Every gynecologist knows that the myoma in itself does not prevent conception and that even in monstrous tumors pregnancy can take place and that the fetus can be carried to full term. There are, however, cases in which the myoma certainly prevents conception, or in case of conception brings about abortion. There is no doubt that in our women who had been married from 5 to 6 years without children the sterility was due to the presence of the myoma since immediately after coitus had been permitted after operation, pregnancy occurred.

As these cases are of importance I shall describe them briefly:

CASE 1. R., aged 30 years, married for 6 years without children. There were no abortions. The patient suffered from diabetes. Operation was performed in May, 1935, with transverse abdominal incision. There were extensive adhesions of the omentum to the tumor and the rectum which had to be freed from the tumor mass. A myoma the size of a child's head situated at the fundus was excised, ten subserous myomas varying in size from a bean to an olive were enucleated. From the left ovary, a follicular cyst was excised, a piece of the ovary was resected and the ovary was reconstructed. Nine months after the operation

[1] In the meantime, 2 more patients have become pregnant so that there is now a total of 9 pregnancies.

the patient became pregnant. The diabetes did not deteriorate during pregnancy. She was treated with insulin. Parturition took place at full term (July, 1936), the child, however, died some days later (adrenal hemorrhage). In January, 1937, she conceived again. Pregnancy and parturition were normal, and the child was healthy.

CASE 2. B., aged 28 years, married for 5 years without having had children. Operation was performed in June, 1935, through a transverse abdominal incision. A left-sided intraligamentary myoma the size of a child's head and some small subserous ones were found. In addition, there was a left-sided ovarian cyst the size of a fist. The ligamentum latum having been divided the intraligamentary myoma was dissected away and removed from the lateral wall of the uterus. The fairly profuse bleeding was checked by knotted sutures, the smaller myomas were enucleated in the typical way. The ovarian cyst was shelled out, the rest of the ovary reconstructed. At the end of operation the patient had a uterus of normal configuration. Subsequent to the operation, menstruation was normal. Eight months after the operation the menses failed to appear. The pregnancy test was positive. On November 3, 1937, there was a normal spontaneous delivery and a normal puerperium.

CASE 3. K., aged 30 years, married for 6 years without children. There were no abortions. Operation was performed in February, 1936, through the transverse abdominal incision. To begin with it seemed hopeless to operate upon this patient conservatively since the uterus showed a large tumor on the posterior wall which appeared to be inseparable from the musculature. In some places the tumor was softened.

Since it was important to the patient that the uterus be preserved, we tried the conservative operation. The tumor was divided sagittally and proved to be extensively cystic and softened in its interior. The tumor reached the uterine cavity. After the tumor had been loosened there remained a large wound area on the posterior wall of the uterus and, in addition, the cavity was opened for a considerable extent. The cavity was now sutured, then the large wound bed was closed in 3 layers. In addition some smaller subserous myomas were enucleated. In this case it was very dubious whether the tubes had remained patent. On the left this certainly was not so, on the right there was a possibility. Eight months after the operation the patient became pregnant. This case, indeed, represents the great possibilities of conservative treatment, since the cavity was opened wide, the entire posterior wall of the uterus was one large wound bed, the tubes were displaced, and it was rather doubtful whether, after the reconstruction of the uterus, the tubes joined the cavity. The occurrence of pregnancy proved that the function of the uterus and the tubes had been preserved. Pregnancy as well as parturition were normal and so was the delivery of the placenta.

CASE 4. S., aged 30 years, married for 11 years without having had children. She had had one abortion. In 1935 salpingography was performed and showed a large uterine cavity. In the beginning the tubes could not be visualized. Only after the use of more powerful pressure they proved to be patent. The operation was performed in April, 1936, through a transverse abdominal incision. There were two fist-sized tumors on the anterior wall, the lower of which had developed antecervically beneath the bladder. The peritoneum of the bladder, therefore, had to be dissected away for a large extent. The removal of a third tumor from the lateral wall was not so simple technically. We did succeed, however, and saw in the transverse section that the center was softened and showed a strange yellowish-brown color. The histological examination carried out during the operation proved that we were dealing with a myoma with central necrosis. In spite of this finding the conservative operation was continued. During the enucleation of the second tumor the uterine cavity had to be opened in an area 2 centimeters in diameter. The uterine cavity was carefully closed with knotted sutures, and then the large myoma bed was closed in three layers. On the posterior wall a myoma of cherry-size also had to be enucleated. The round ligaments were fixed to the anterior wall of the uterus so that the uterus was anteflexed and the areas of suturing were covered. This case demonstrates that even necrosis of the myoma is no reason for abstaining from the conservative operation. The fact that the patient became pregnant one year after operation demonstrated that the uterus was normal in function. Parturition, delivery of the placenta, and puerperium were normal.

CASE 5. G., aged 32 years, had been married for 11 years without having had children. She had had one abortion. Operation was performed in January, 1936, with transverse abdominal incision. We found a left-sided intraligamentary tumor the size of a child's head, tightly adhering to the edge of the uterus. The parametrium had to be broadly divided and the tumor cut out. The removal from the lateral wall of the uterus was difficult. However, hemorrhage from the left uterine blood vessels occurred which was controlled by ligating the vessels. In the uterus itself there were twelve smaller myomas which were situated partly intramurally, partly subserously. They were enucleated in the typical manner and the beds of the myomas were sutured. There remained a well formed uterus with patent tubes. Six months after the operation pregnancy occurred with subsequent normal birth.

CASE 6. Sch., aged 30 years, had been married for 6 years without having had children. She had had three spontaneous abortions. The operation was performed in April, 1936, with transverse abdominal incision. Several small cherry-sized subserous myomas were enucleated. In May, 1937, menstruation failed to appear. The pregnancy test was positive and the course of pregnancy, parturition and puerperium was normal.

CASE 7. W., aged 32 years, had been married for 5 years without children. She had had three spontaneous abortions in the third month and one premature delivery in the seventh month. The operation was performed in October, 1936, with transverse abdominal incision. We found a myomatous uterus consisting of several nodular masses, a fist-sized tumor on the anterior wall, a plum-sized subserous tumor on the posterior wall, both on the right and on the left sides nodules the size of a cherry. On the right the tumor reached a point near the tubal orifice; the tumor, however, could be dissected out in such a manner that injury to the tube was avoided. Seven months after the operation the patient became pregnant; parturition as well as puerperium were normal.

No doubt, parturition is fraught with the danger of rupture of the uterus following the conservative myomectomy. I did not, however, encounter a rupture of the uterus following this operation. The important points are first to select the right type of incision in order to spare the musculature of the uterus to the utmost degree and second to suture the myoma beds perfectly. The 7 cases described all had normal deliveries, and the delivery of the placenta was normal in spite of the fact that in some of the cases the uterine cavity had been opened. In any

case, we must take care that the women who have had a conservative myoma operation should be confined in the hospital where at any moment an operative delivery can be performed.

The objection which can be made to the conservative operation is that we do not radically remove the disease, that a new myoma may develop from a remaining focus. Theoretically, this is undoubtedly correct. Practically, however, recurrence proved to be a rare event. Among the patients whom I operated upon in Palestine I saw only 2 cases of recurrence.

There are apparently only a few hospitals where the conservative operation is done as a matter of principle. Such an experienced surgeon as Bonney, who uses the conservative operative method chiefly reports from his immense material of many years 2.3 per cent of recurrences. These excellent results can be obtained only by radically operating, i.e., by removing *every* perceivable and palpable myoma nodule. He who fears, from technical reasons, the removal of nodules from a dangerous site, has not mastered the technique of the conservative operation. The women whom I have treated here readily took upon themselves the risk of a relapse of the uterus, thereby to preserve the possibility of conception. After operation, they felt that they were real women. Relapse does not usually occur until years have elapsed, perhaps not before the woman is at an age when irradiation is the treatment of choice.

SUMMARY

1. Conservative myomectomy has been used on principle. Of 67 women in a sexually mature age 40 were operated upon conservatively (59.7 per cent). Of the last 10 cases 9 were operated upon conservatively.

2. The size, the number, the site or even benign degenerative changes in the myoma do not contra-indicate the use of the conservative operative method.

3. After the conservative operation conception took place in 7 patients, in which the pregnancy as well as the parturition and puerperium were normal.

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MADELUNG'S DEFORMITY AND ASSOCIATED DEFORMITY AT ELBOW

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THE growth deformity at the distal end of the radius, to which the name of Madelung has been attached, is described with considerable anatomical variation. Four typical additional cases are recorded in this report. Two of these were observed and treated for a period of 4 years prior to the termination of growth in the bones of the forearm. The remaining two were more recently discovered, and are to be treated in the near future. A fifth case, which presents many of the characteristics of the deformity, is included for completeness. Three separate surgical procedures were necessitated in the treatment of one of these patients. Two of the others are of particular interest because of associated deformity in the proximal end of the radius, with changes in the elbow joint.

HISTORY AND ETIOLOGY

The term, Madelung's deformity, predominates, in foreign literature, as a favorite one describing this entity. In addition, one finds Dupuytren-Madelung disease, Madelung-Duplay, radius brevior, congenital dysmorphosis of the wrist, radius curvus, and more recently inferior radiocubital chondrodysplasia. American and British authors have designated this deformity as idiopathic progressive curvature of the radius, a spontaneous forward dislocation of the wrist joint, carpus varus, and spontaneous subluxation of the wrist. It is necessary to distinguish between Madelung's deformity and what is frequently referred to as Madelung's disease. The typical deformity is curvature of the distal half of the radius in a combined volar and ulnar direction, shortening of the forearm, prominence of the distal end of the ulna, and volar subluxation of the hand at the wrist.

The deformity has been recognized at all ages. The etiology has been ascribed to fractures, specific disease involving the distal radial epiphysis, congenital dislocation, arthritis, congenital and adolescent rickets, osteochondritis, osteofibroma, and traumatic separation of the epiphysis. Madelung's disease, however, must be limited to those in which the deformity occurs with pain in early adolescence, appears without trauma or infection, involves the distal growth center of the radius, and terminates with early closure of this epiphyseal growth line. It is well to recognize that this is the clinical entity which Madelung described in 1878, and that the typical deformity following the disease is simulated from various known causes at other ages.

Madelung recognized the disease as a disturbance in growth, which develops spontaneously, never before 13 years and rarely after 23 years of age. He attributed the deformity to the powerful action of the flexors of the forearm, and mentioned primary weakness of the bones, or disturbance in nutrition as predisposing factors. Redard, in 1892, first recorded the opinion that the deformity resulted from a growth disturbance in the distal radial epiphyseal cartilage. This one factor has held pre-eminence over the possibility of rickets, trauma, local inflammatory disease, and trophic disturbances as possible etiological factors. The condition occurs seven times as frequently in females as in males. Two-thirds of the cases have bilateral deformities. Stetten reports that one-third of the cases have a definite hereditary factor. The symptoms of the disease almost always appear in early adolescence. These facts limit the true etiology of the entity to an almost unknown factor. Therefore, if we speak of it as a disease, we must accept it as one of unknown etiology.

Recent German writers (Beder and Heinismann and Cserey-Pechany), nevertheless, have reported isolated cases of the deformity associated with delay in the onset of menstruation, and attribute its cause to disturbance in ovarian function. Our findings would not support this view. The occurrence of the deformity in males, as has been reported (8) could not be accounted for by such a theory. There has been no consistent relationship between this single localized growth disturbance and other growth disorders and deformities having a similar age frequency.

PATHOLOGICAL MECHANISM

The actual growth disturbance, which precedes the appearance of the deformity and causes pain

Fig. 1. Case 1. Deformity in right wrist as compared to left at age of 13 years and 3 months.

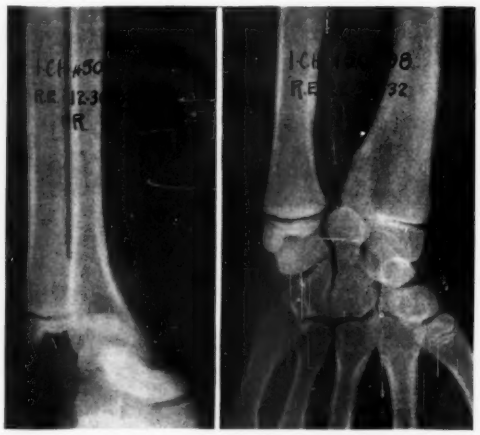

Fig. 2. Case 1. Right wrist showing involvement of radius, separation and dorsal displacement of ulna, and wedging of carpals, at 12 years and 10 months.

in the wrist, probably has its onset months and perhaps years before recognition of the deformity. There is a considerable variation in the degree of the deformity, as described by Schnek, in which the extreme is the "konsolen" form, with an intermediate form in comparison to the normal radius. This variation readily accounts for some cases in which the deformity is not recognized until adult life, when only a meager history of pain in the wrist during adolescence can be elicited. Claiborne and Kautz have recently called attention to the fact that incomplete and latent deformities occur in addition to those manifested clinically by pain and impairment of motion in the wrist. The earliest recognized cases have shown partial closure of the distal epiphyseal growth line on the volar and ulnar portions. With continued growth in the remaining portions of the epiphyseal line, the typical curvature of the distal part of the radius results. Retardation of growth rate must precede premature closure of the growth plate, if one is to account for the curvature in the diaphysis. This is the basis for the theory of disproportionate growth for a period of months or years before the onset of pain. Pain occurs only when the deformity is sufficient to distort or distract the distal radio-ulnar articulation.

The normal slight volar and ulnar angulation of the distal articular surface of the radius is gradually increased. This continues as long as any portion of the epiphyseal growth line exists as such, and the distal end of the radius is protracted away from the ulna carrying the carpus and hand with it. An inverted V shaped arrangement of the proximal row of carpals results. The lunate is at the tip of the wedge formed by the articular surfaces of the radius and ulna. Frequently there is a rather marked change in the shape of the affected carpals, and often a longitudinal separation of the two rows, following a line between the os lunatum and os triquetrum and between the os capitatum and os hamatum. Premature closure of the radial epiphyseal growth line occurs. The ulna continues to grow, and projects dorsally and distally from the subluxated carpus and hand.

CLINICAL SYMPTOMS

Pain and limited motion of the carpus and distal radio-ulnar articulation are the early symptoms, except in the milder degrees of the deformity, in which only the distortion of the wrist is noted. The earlier the onset of pain, the more severe is the deformity which follows. Any active use of the hand apparently aggravates the pain. Such a combination of symptoms is justifiably accounted for, in the mind of the child or its parents, by a strain or minor injury. The pain is usually constant in character. Only slight relief can be expected from the most efficient fixation. The hand deviates to the ulnar side. The prominent distal end of the ulna may be replaced to the level of the wrist by pressure but returns to its dorsal position when pressure is released. Viewed on a lateral plane, the hand is subluxated toward the volar surface, on the forearm.

TREATMENT

Pain is the most constant symptom necessitating therapy. Almost invariably authors mention

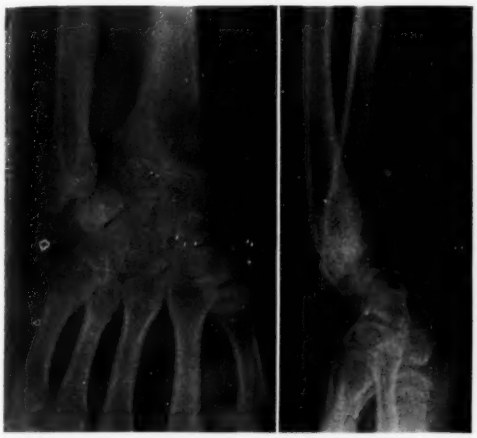

Fig. 3. Case 1. Partial closure of the distal ulnar epiphysis has occurred 10 months after operative epiphyseal arrest. Age, 14 years, 2 months.

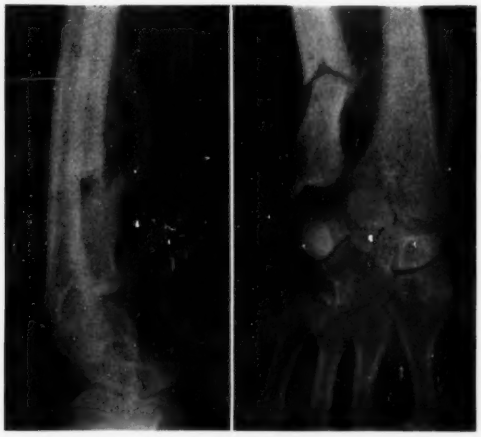

Fig. 4. Case 1. Four weeks after second operation—osteotomy of ulna. Note improvement in relationship of radius and ulnar as compared with Figure 3. Age, 15 years, 4 months.

the failure of protective appliances in its relief. The deformity at the termination of growth is readily corrected by osteotomy.

Phemister first advocated epiphyseal arrest at the distal end of the ulna to retard its growth. Burrows has combined resection of the juxta-epiphyseal portion of the shaft of the ulna and excision of the ulnar epiphyseal disc with simultaneous linear osteotomy of the radius before termination of growth in this bone. Lewin has excised the distal end of the ulna, at a point corresponding to the length of the radius, to correct the inequality in the length of the two bones. Ovarian hormones have been administered with alleged good results (4), but the success of such treatment must obviously depend on the rapidity of development and degree of deformity in an individual case. Schnek has used corrective osteotomy of the radius alone, in cases in which the disproportion in the length of the bones was not a major factor in the deformity.

Case 1. R. E., a schoolgirl, 13 years of age, was brought to the out-patient orthopædic clinic of the Indianapolis City Hospital, on December 30, 1932. Her mother stated that the child had a painful deformity of the right wrist, which was first noticed 3 months previously. A sprain during play at school was mentioned as a possible cause. The girl denied any swelling or disability of the wrist at the insidious onset of the pain. This pain, never throbbing in character, had been constant and was aggravated by use of the hand in playing the piano and school work.

A study of her previous history did not disclose any record of prolonged illness or infectious disease. No bone or joint deformities were present in either parent, or her one sister. Menstruation had not started and the secondary sexual characteristics were not yet in evidence.

There was ulnar deviation of the hand, with a curvature of the radius, the concavity of which was toward the volar and ulnar surfaces of the forearm. There was 2 centimeters shortening of the forearm and hand, as compared with the left. The distal end of the ulna protruded dorsally from the wrist (Fig. 1).

No signs of inflammatory processes about the wrist were present, and signs of systemic disease contributing to her complaint, were not found. Roentgenograms made that day disclosed changes in the wrist consistent with a diagnosis of typical Madelung's deformity (Fig. 2). It was noted that the closure of the ulnar portion of the distal radial growth line was continuous with a distortion of bony

Fig. 5. Case 1. End-result of ulnar osteotomy. Ulnar epiphyseal line closed; radial partially open. Age, 15 years, 9 months.

a b

Fig. 6. Case 1. a, Deformity present at termination of growth and before final corrective osteotomies. Age, 17 years; b, Left forearm and wrist for comparison with Figure 6a.

trabeculæ and contour, which extended proximally for a distance equal to the width of the bone at that level.

A volar plaster splint was applied for fixation of the hand in a neutral position. At the end of 3 weeks, this was removed and reapplied. At the end of 10 weeks of fixation, March 16, 1933, there had been no noticeable relief of pain. Roentgenograms were made of both wrists, April 24, 1933, for comparative purposes. The retardation in longitudinal growth of the right radius, as compared with the left, was recognized. At this time, some relief from pain was noted, after prolonged protection of the hand and forearm in a sling.

On June 1, 1933, the patient was hospitalized. Routine laboratory examination failed to disclose any evidence of systemic disease or infection. On June 8, 1933, under general anesthesia, an epiphyseal arrest by excision of the distal ulnar epiphyseal growth line was performed. A volar plaster splint was again applied, for fixation of the hand and wrist. Roentgenograms made June 13, 1933, revealed a slight increase in the deformity. Fixation of the extremity was maintained for four weeks following the operation.

The patient was free from pain in the wrist for 8 to 10 months following this surgical procedure. She returned in March, 1934, with recurrence of pain and an increase in the deformity. She reported that menstruation had started, but at the age of 14 years, this delay was consistent with that of her mother and sister.

Roentgenograms made at this time (Fig. 3) revealed a partial closure of the distal ulnar epiphyseal growth line, and changes in the distal end of the radius. Protection for a period of 2 months was maintained, with only slight relief of pain.

During the next year there was a recurrence of pain and an increase in the limitation of motion involving rotation of both the forearm and the wrist proper. On April 29, 1935, under local anesthesia, resection of 2 centimeters of the shaft of the ulna just proximal to the wrist joint was performed. Immediate relief from pain followed this procedure. The distal fragment of the osteotomized ulna dropped to the level of the radius, and the radio-ulnar articulation was restored (Fig. 4). Bony union occurred at the site of the osteotomy in 3 months. The subsequent appearance of the wrist is disclosed in roentgenograms taken January 12, 1936 (Fig. 5). The patient remained free from pain, although roentgenograms made April 12, 1936, 1 year after the second operation, revealed still greater increase in the deformity and closure of the remaining small portion of the distal epiphyseal growth line of the radius. The radio-ulnar articulation and the approximation of the carpals were fairly well restored by the ulnar shortening procedure. The patient was then 16 years of age.

On February 17, 1937, at 17 years of age, she reported complete freedom from pain since the surgical shortening of the ulna, and desired correction of the remaining deformity. Roentgenograms made then (Fig. 6a) disclosed cessation of growth of the radius and ulna, with closure of the distal epiphyseal growth lines. The deformity at this time was of considerable degree, as is shown in Figure 7. There was 4.5 centimeters shortening of the right forearm and hand. At this time, under general anesthesia, incomplete linear osteotomies were performed at the maximum points of curvature of the radius and ulna. There was partial healing with satisfactory alinement by March 22, 1937. Protection was applied to the arm for a period of 8 weeks. A good cosmetic result was obtained (Figs. 8a and b). The end-result as shown roentgenographically was satisfactory (Fig. 9). The changes in angulation of the articular surfaces of the distal ends of the radius and ulna are shown diagrammatically in Figure 10.

Fig. 7.

Fig. 8a.

Fig. 8b.

Fig. 7. Case 1. Gross deformity at termination of growth period and shortening in the right forearm.

Fig. 8. Case 1. a, Illustrating the gross appearance and cosmetic results following the final osteotomies. Note the lack of curvature in the forearm. b, Illustrating the difference in length between the two forearms and the reduction in curvature following the final osteotomies.

From a functional standpoint, the right forearm was markedly improved by the corrective osteotomies, although there was a 20 per cent limitation in rotation of the right as compared with the left, and the arc of motion at the wrist was restricted to 75 per cent of that on the left. Throughout the latter 2 years of the progress of her deformity, this patient played the piano with sufficient skill to hold a place of honor in her school orchestra, and has since followed the same vocation with a private orchestra.

CASE 2. H. A., a schoolgirl, 13 years of age, was brought to the out-patient orthopædic department of the Riley Hospital, Indianapolis, on April 26, 1933. Her mother stated that she had had pain in her right wrist, associated with a slight deformity, for 1½ months. The onset of the pain was insidious and was not associated with any known trauma. The pain had increased in severity since its onset. This symptom was never of sufficient severity, however, to warrant protection. No other joint had been painful, and there were no systemic symptoms preceding the onset of her complaint. The mother corroborated the statement that the patient had suffered no unusual accident during the 2 years prior to the onset of her trouble. Prolonged use of the hand at school and light housework were definite aggravating factors.

A study of her previous history failed to reveal any evidence of serious illness other than childhood diseases. Her parents and one sister were free from any skeletal deformities and were of average height and weight. Menstruation started at 11½ years and the secondary sexual characteristics were normal.

Prominence of the distal end of the ulna and ulnar deviation of the right wrist were noted. There were no signs of swelling or inflammation in the wrist. Similar changes were noted in the opposite wrist, but no complaint of pain in the left was made. Limited motion in the right wrist was consistent with the deformity. A moderate cubitus valgus was noted.

Roentgenograms of both wrists disclosed partial closure of the distal radial epiphyseal growth lines and other changes conforming to those of Madelung's deformity (Fig. 11a and b). The changes were more marked on the right. Epiphyseal arrest in the distal end of the right ulna was advised, but surgical treatment was refused. Limitation of

Fig. 9. Case 1. Showing the roentgenographic end-result of the corrective osteotomies 8 weeks after operation.

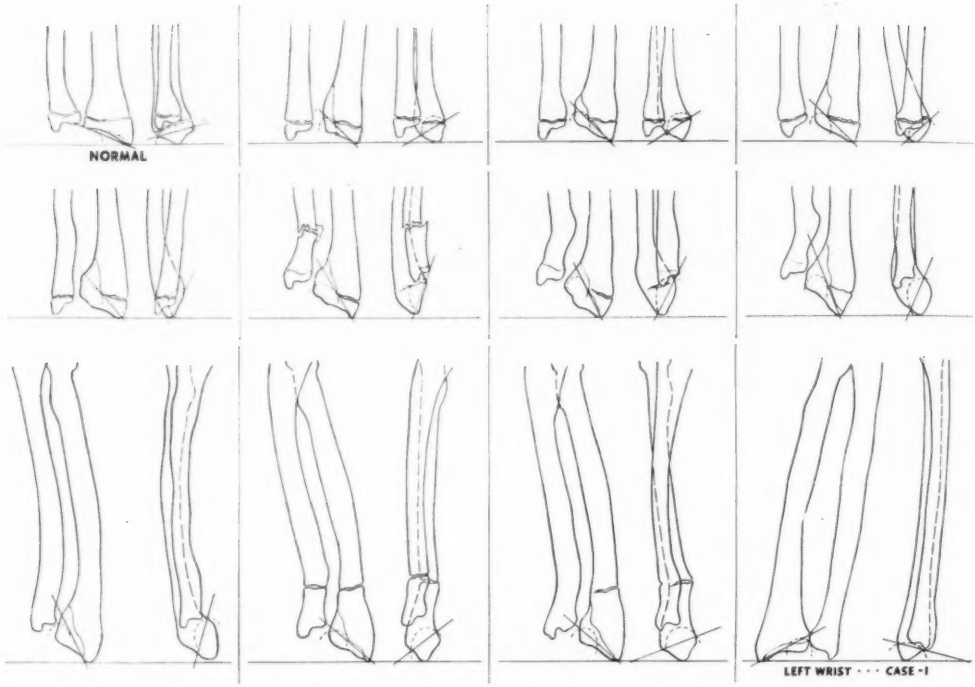

Fig. 10. Case 1. Chart showing diagrammatically the changes in angulation of the distal articular surface of the radius at the stages in the handling of this patient previously illustrated. The first diagram is of a normal right wrist at 13 years of age. The last is of the left forearm in Case 1 at 17 years of age.

the use of the forearm consistent with the pain present was advised as an alternative.

Re-examination on November 5, 1935, revealed the history that the pain had subsided after a few months and had remained absent. A slight increase in the deformity was noted. There was definite anterolateral curvature in the left radius also.

It was not until March 30, 1937, that roentgenograms were again obtained on this patient, who was then 17 years of age. The distal epiphyseal line had closed in both the radius and ulna, with typical deformities of Madelung's type. Rotation of each forearm was limited to an arc 120 degrees. There was instability at each elbow in its lateral plane and a definite bony "click" upon abduction of the joint. Full length studies of the radius and ulna of both arms, at this time, revealed atrophy of the proximal end of the radius, and distraction of the head of the radius from the elbow. Hypertrophy of the fused capitellum was noted. These changes are shown diagrammatically in Figure 12a and b. Cubitus valgus of 30 degrees and lateral instability of 5 degrees was present in each elbow.

Case 3. C. J., a school girl, 14 years of age, was brought to the out-patient orthopædic clinic of the Roper Hospital, Charleston, on June 13, 1933. Her mother stated that the girl had had pain and a noticeable deformity of the left wrist for 3 months. She had suffered a somewhat severe fall at school, with injury to her knee and possible injury to the wrist. The injury to the knee was immediately painful and she was kept in bed for the following month. During this time, she first noticed slight pain in the left wrist, which gradually increased prior to admission. The pain was constant and increased with use of the hand in household tasks. The deformity gradually increased and was rather marked on admission.

A study of her previous history revealed childhood diseases, a partial facial paralysis on the left side at 6 years of age, and no serious illness since childhood. There was a definite history of exposure to a cold draft to account for the facial paralysis, and there was only a slight residual paralysis in the left side of the mouth. Menstruation had started at 12 years, and the secondary sexual characteristics were normal. There was no skeletal deformity in either parent and an older sister.

The deformity present was an ulnar deviation of the wrist and hand and some volar displacement with prominence of the distal ends of the radius and ulna dorsally. Roentgenograms made on that day revealed the changes in the radius and ulna characteristic of Madelung's deformity. A support to the forearm and protection of it was advised and carried out for approximately 3 months. There was no relief from pain and no improvement in the deformity. Surgery was then advised, but was refused.

The patient was next seen on December 22, 1937, at which time roentgenograms (Fig. 13a, b, and c) were made. Her only complaints then were of slight pain in the left wrist after long hours of work. As will be readily seen, the

a b

Fig. 11. Case 2. a, Anteroposterior view of both wrists showing changes typical of Madelung's deformity, more marked on the right. Age, 13 years, 2 months. b, Lateral view of both wrists at same age.

right wrist was also involved, but the patient stated that she had never had pain in it. The changes were typical of Madelung's deformity, being much more marked on the left. There is a definite shortening—3 centimeters—of the left forearm as compared with the right.

The deformity present in the left forearm is a marked ulnar deviation and volar displacement of the wrist and hand. There is limitation in rotation of the forearm and extension and abduction of the wrist and hand. Corrective osteotomies of the radius and ulna are to be performed in the near future, since the end of the growth period has been reached.

CASE 4. J. C., a graduate nurse, 21 years of age, presented herself at the x-ray department of the Roper Hospital, Charleston, on December 30, 1937. She complained of painful deformities of both wrists present since adolescence. This patient stated that pain was first noticed in the left wrist when she was 12 years of age. Shortly thereafter, she noticed pain in the right wrist, though it was never as constant as that on the left. The deformities became noticeable when she was 13 years of age and gradually increased until she reached 18 years of age. Since that time, there has been no apparent change in the appearance of either wrist. The pain was never very constant in either wrist, but always more marked on the left, and always aggravated by tiring work, such as knitting. She never had sufficient discomfort to wear any kind of supportive device. During her years of nurses' training in this hospital she was repeatedly advised to have surgical attention but always refused.

A study of her past history revealed the usual childhood diseases, but no serious illness since early childhood. Menstruation started at 12 years of age, and the secondary sexual characteristics appeared normally. There is no skel-

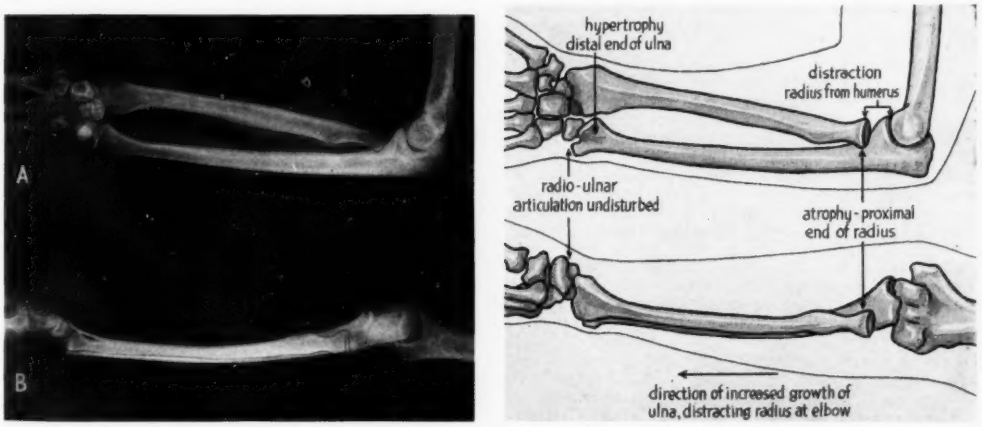

Fig. 12. Case 2. a, left. Retouched roentgenogram to illustrate changes at elbow, i.e., atrophy and distraction of head of radius, and hypertrophy of capitellum. b, Diagrammatic representation of Figure 12a.

a b c

Fig. 13. Case 3. a, Both forearms in supination. Note the increase in deformity on the left with marked shortening of the radius, and the slight deformity on the right. Age, 18 years. b, Right forearm in lateral and pronated positions. Compare with Figure 13a and c. Age, 18 years. c, Left forearm in lateral and pronated positions. Compare with Figure 13a and b. Age, 18 years.

etal deformity in either of her parents. Her one sister, older, has a slight prominence of the distal end of the left ulna, but no other signs of deformity. Unfortunately, this sister would not consent to have roentgenograms made of her wrists.

This patient has a marked curvature of each radius, with the concavities toward the volar and ulnar surfaces, an ulnar deviation of each wrist and hand, a volar displacement of the wrists, and a marked prominence of the distal end of each ulna. There is a definite loss or limitation in rotation in each forearm. This is more pronounced on the left, where there is at least 60 per cent reduction in ability to supinate the forearm and hand. There is limitation in abduction and extension of the wrist and hand, somewhat more evident on the left.

The full length roentgenograms of each forearm (Fig. 14) reveal the changes characteristic of Madelung's deformity. They are perhaps a little more pronounced on the left. On the right, however, there is definite distraction of the proximal end of the radius from the elbow, and some overgrowth of the capitellum, as noted in Case 2. The exostoses so frequently reported in the literature as occurring on the ulnar side of the lower or distal end of the radius, are clearly demonstrated in this patient. The distal epiphyseal growth lines have completely closed and become obliterated, as one would expect.

This patient cannot recall any trauma which might account for the beginning of these deformities. She has been reluctant about having any attention called to her wrists, but has finally consented to have osteotomies in the near future, for the correction of the deformities. The end-results on this patient and Case 3 will be reported at a later date.

Case 5. A. L., an office worker, 26 years of age, presented herself at the x-ray department of the Methodist Hospital, Indianapolis, on August 20, 1937. She stated that she had had slight pain and deformity of both wrists for many years. The deformities first became noticeable when she was 11 years of age. There was no definite history of previous trauma to either wrist or forearm. The deformity in the left wrist increased slightly in the following year and became painful after exertion. Her physician recommended the wearing of braces for each wrist, which she did for 2 years. These did not correct the deformity or relieve the occasional pain.

A study of her previous history revealed no evidence of serious illness since early childhood. Menstruation began at 13 years of age, and the secondary sexual characteristics developed normally. There was no skeletal defect in her father. Her mother had always had rather large wrists, which became painful at times after arduous labor. No other relatives were known to have deformities of this character.

This patient has a definite prominence of the distal ends of the radius and ulna, more noticeable on the left; a slight ulnar deviation of the wrist and hand, also more marked on the left; a slight volar displacement of the wrist and hand: and an increase in the curvature of the lower one-half of each radius. There was only slight limitation in rotation of the forearms, but definite limitation in extension of the wrists and hands, and some limitation in abduction. At that time, she had pain only after excessive use of the hands as in knitting. There was not sufficient deformity or disability present to consider operative interference.

Roentgenograms of both forearms and wrists (Fig 15) reveal many of the characteristic changes of Madelung's deformity. They are more marked on the left. There is an increase in curvature of the distal half of the radius, with concavity toward the ulnar and volar surfaces. There are distinct increases in the angulations of the distal articular surface of each radius. There is some dorsal displacement of the distal end of each ulna, and a slight volar displacement of each wrist. The changes are not as extreme as those seen in other patients reported here, but probably represent an incomplete or frustrated form of this type of deformity.

Fig. 14. Case 4. Both forearms in pronation, showing typical Madelung's deformities bilaterally. Exostoses on the radii are clearly shown in this case. Age, 21 years.

Fig. 15. Case 5. Left forearm in pronation and a lateral position. The changes are quite typical of Madelung's deformity.

The first three patients presented themselves at approximately the same age and within a few months after the onset of clinical signs indicating Madelung's deformity, but showed striking variations in the development of their deformities. No demonstrable cause for the partial arrest of growth and premature closure of the distal radial epiphyseal growth line was found in either of the first two. The history of trauma, in the third case, was indefinite as far as the wrist was concerned, and certainly of debatable significance in the light of later discovery of involvement of the opposite wrist. The last two patients presented themselves at later ages, when the deformities present had become stationary.

No other bony anomalies were found in any of these patients, and thorough search, including roentgenographic examination, was made in each case. In only one case was there any familial history that was even suggestive of hereditary factors. All patients observed with the deformity were females. All had normal sexual development during adolescence, with the onset of menstruation being slightly delayed in only one case, in which this was apparently familial. One could not say that there was any evidence of deficiency in ovarian function in any of these patients.

On one patient, Case 1, three separate surgical procedures were done. Epiphyseal arrest, and later resection of a portion of the diaphysis of the ulna near the wrist, were successful in obtaining a pain-free joint. It must be admitted that the second was the more effectual of the two procedures, but conservatism prompted the less radical first operation. The final osteotomies were done for cosmetic purposes, and contributed materially to increase the function of the deformed wrist.

In Cases 2 and 4, there is demonstrated a previously undescribed growth defect in the radius, associated with Madelung's deformity. This is an atrophy of the proximal end of the radius, and distraction of it from the elbow, with hypertrophy of the capitellum, but no functional impairment of the joint. This phenomenon readily accounts for the comparative freedom from pain at the wrist in spite of considerable deformity there. The cubitus valgus and the hypertrophy of the capitellum present in these cases, are no doubt physiological compensation for the deficient length of the radius.

It is logical to assume that, in these patients, distortion of the distal radio-ulnar joint did not occur during the progressive growth of the deformity, because fairly normal relationships were maintained by the wrist ligaments, and distraction of the radius from the elbow followed the continued growth of the ulna at the wrist. No pain apparently accompanied the changes at the elbow. The shortening of the radius was compensated for by its being drawn away from the elbow, rather than remaining as a fixed element there and allowing projection of the ulna at the wrist.

SUMMARY AND CONCLUSIONS

Madelung's disease is an entity of unknown etiology, involving the distal end of the radius.

There is a primary disturbance in the bone in this region, followed by pain and the development of a deformity—Madelung's deformity—in the adolescent years. The specific portion of the radius involved is the region of the distal epiphyseal growth line, where there is growth disturbance and premature closure, with resultant production of deformity and pain. The pain is the result of distortion, by the deformity, of the distal radioulnar and carpal articulations.

The severity of the pain is directly proportional to the degree of the deformity, except in those cases in which the element of distraction of the head of the radius from the elbow enters, as illustrated in 2 cases here reported.

Certain cases do not present all of the signs of the disease and deformity but undoubtedly represent an incomplete form rather than a pseudo-Madelung's deformity. In some cases, the deformity may be simulated following injury or known disease, but these cannot be classified as true Madelung's disease.

Resection of a portion of the diaphysis of the ulna near the wrist joint, is the most effective means of relieving the pain as it corrects the distortion of the joints. Corrective osteotomies at the points of greatest curvature, after growth is completed in both bones, will reduce the deformity and increase the function of wrist and hand.

The authors wish to thank the departments of roentgenology and illustrations of the Indiana University Hospitals, the department of roentgenology of the Indianapolis City Hospital, the departments of roentgenology and illustrations of the Methodist Hospital, Indianapolis, and the department of roentgenology of the Roper Hospital, Charleston, for assistance in the preparation of illustrative material used in this article.

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OPEN REDUCTION OF FRACTURES WITH SPECIAL BONE APPROXIMATOR

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A CONTROVERSY exists among the advocates of open reduction in the treatment of fractures and those who insist that all fractures, with very few exceptions, should be treated by the closed method. This controversy is clearly brought out by quoting divergent viewpoints of outstanding surgeons.

Dr. Lorenz Boehler, of the University of Vienna, says: "The most unfortunate innovation in the treatment of recent fractures is the routine exposure and reduction by open operation, particularly if this practice is carried out by inexperienced persons without special indications, with defective appliances, and with the application of large metal foreign bodies. Thousands of human lives have been sacrificed by these procedures and many more have been crippled by them."

Dr. W. O. Sherman, of Pittsburgh, in his recent fracture oration before the Clinical Congress of the American College of Surgeons in Chicago said: "For the past 30 years severe criticism has been leveled at those who have used steel bone plates, screws, nails, etc. Many of the leading critics in personal interviews have admitted to me, that they never had any experience whatsoever with steel plates, screws, or nails in the treatment of acute fractures, and that their opinion was based entirely on the poor end-results which they have seen in cases in which the operation was imperfectly or poorly done. Since the World War there has been a 'mass production' of bone and joint specialists many of whom lack general surgical training. A surgeon who requires three hours to do an operation that should be done in forty-five minutes should not attempt it."

In my opinion both men are correct. In recent years the tendency of open reduction in the treatment of fractures has increased considerably. The open reduction of a fracture made by a competent surgeon who follows scrupulously the non-contact technique of Lane, and practises a rigorous asepsis, in my opinion takes no more risk than when he operates on a chronic appendix. Poor results in the operative treatment of fractures are due to incompetency because of improper selection of cases, poor surgical technique, and asepsis. Operating treatment involves great danger if done when the soft tissues have not had sufficient time to recuperate from the trauma caused by the fracture and transportation. Operating in the presence of edema, blebs, and excoriations of the skin is a mistake by which the life of the patient is jeopardized.

The majority of fractures can be treated by the closed method. However, in a good number of fractures the surgeon is unable to get a perfect reduction by the closed method. Examples are:

1. Fractures involving joints in which the short fragment acts as a loose body, i.e., the upper end of the humerus and radius.

2. Fractures with distractions, patella, olecranon, etc.

3. The intracapsular fracture of the neck of the femur in which the best results are being obtained by following the teachings of Smith-Petersen as advocated by him, Moore, Cubbins, and others.

4. Fractures with badly displaced fragments in which interposition of soft tissue takes place.

5. Lastly, every surgeon will have to face the problem of the fracture coming to him between 2 weeks to several months or years after its occurrence.

Every surgeon doing fracture work has had the experience of seeing a patient with a fracture of the femur with strong bony union in a poor position with an over-lapping of one inch or more; or with a fracture of the lower third of the humerus mal-united with marked angulation and stiff elbow joint, etc.; with fractured tibia with 1 or 2 inches of shortness, etc.

For several years we have been employing the technique we are about to describe in operative treatment of acute fractures of the long bones:

1. *Time.* As a rule we operate between the twelfth and fifteenth day after the occurrence of the fracture. During these first 2 weeks we try to do a closed reduction but if we fail to obtain the proper position of the fragments, we do not hesitate to operate. During those 2 weeks the patient is prepared for operation, and the soft parts have had a chance to rehabilitate themselves of the original trauma.

2. *The preparation.* The day before the operation, the operative field is thoroughly cleansed with soap and water followed by alcohol, and is covered with a sterile towel.

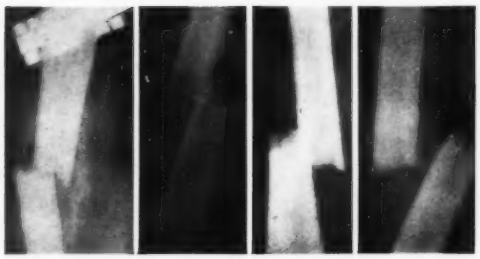

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Fig. 1a. Transverse fracture of right femur through middle third, with strong bony union in poor position, 3 weeks after accident.

Fig. 1b. Transverse fracture of right femur of the lower third, 25 days after accident with strong bony union in very poor position.

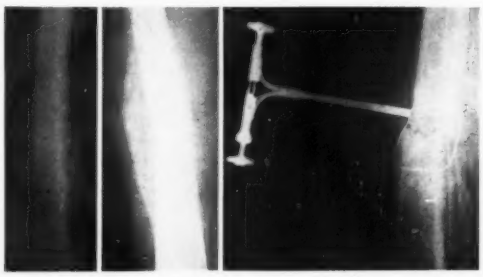

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Fig. 3a. Two months after operation. Both bone approximator and wire removed with perfect results.

Fig. 3b. Same case 1 month after operation, with fragments in very good position and strong bony union. Wire and approximator removed 6 weeks after operation.

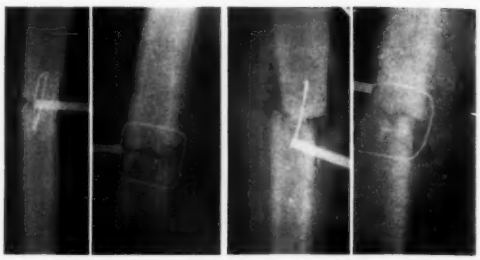

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Fig 2a. Same case 2 weeks after operation. Note perfect position of fragments.

Fig. 2b. Same case 2 weeks after operation showing fragments in good position.

3. *Technique of operation.* At the time of operation the field is prepared again with tincture of iodine followed by alcohol and finally painted with a mixture of both. The surgeon personally drapes the field. He wears two pairs of gloves, and discards the outer pair when the patient has been draped and the towels affixed with clips to the edges of the wound. Under no circumstances should the fingers, instruments, or surgical material used in the operation touch the skin since this constitutes a potential source of contamination. The knife used to make the incision through the skin is discarded immediately and a new knife is used for the deeper structure.

The smallest possible incision is made and about one half inch of each fragment is exposed. Stripping the fragments of their periosteum or bringing the fragments out in the operative field should not

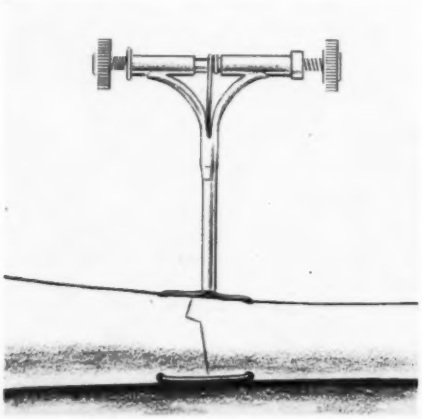

Fig. 4. Drawing of bone with transverse fracture showing bone approximator with wire in place. Note how fragments are kept in perfect position.

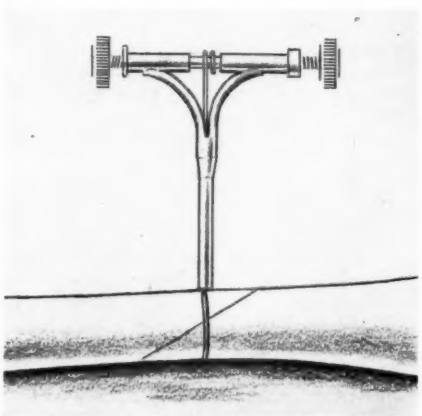

Fig. 5. Drawing of bone with an oblique fracture showing wire wound around fragments. It is unnecessary to pass wire through the fragments.

be done. Reduction of the fracture is carried on by traction and manipulation.

A hand driven drill to which is affixed a fine Kirschner wire is used to drill a hole in each fragment, about ½ inch from the site of the fracture. A steel wire (Babcock's No. 18 or No. 22) is passed through the hole drilled in one fragment, then across the site of the fracture, finally passing the wire through the other hole in the opposite direction. The two ends of wire emerging from the wound are passed through the cannula of the bone approximator which we use; the fragments are set in good position and the knob of the instrument is turned until enough pull is exerted by the wire to keep the fragments in perfect position (see Figs. 1 to 4, a and b).

In the oblique type of fracture it is not necessary to pass the wire through the fragments. In such cases the wire is wound around the fragments, a small groove is made in the bone (Fig. 5).

A clean operative field is of the utmost importance so that perfect hemostasis is carried out all throughout the operation. The wound is closed in layers with simple No. 1 catgut and the skin is closed in the usual manner.

4. *Postoperative treatment.* According to the type of fracture the postoperative handling may be done by application of cast, the use of Russel traction, Thomas splint with Pierson attachment, etc. The position of the fragments are checked by means of x-ray, 24 hours, 2 weeks, and a month following operation. Once the fragments have been accurately reduced and immobilized, active movements are started on the second postoperative day, since this increases the circulation and stimulates the callus formation. If at the end of a month the x-ray film shows that there is enough callus to keep the fragments in position, the instrument is pulled out and the steel wire is removed. If the x-ray film shows that there is not sufficient callus, then another 2 weeks of waiting is necessary. Lately in cases of fracture of the lower limb we have made our cases crutch ambulatory by applying a cast which includes the bone approximator (see Fig. 6). Naturally, this reduces considerably the time of hospitalization ordinarily required.

The bone approximator is easily removed, but for the removal of the steel wire, a strong pull is required. Sometimes the wire is left in place for several days after the bone approximator has been removed.

Fig. 6. Patient with transverse fracture of right femur. Crutch ambulatory, 1 week after operation. The approximator has been included in the cast.

ADVANTAGES

1. Absolute reduction is maintained.

2. No foreign body is left in the bone since both wire and approximator are removed in between 4 to 8 weeks, thereby eliminating a secondary operation.

3. Since a very small portion of bone is exposed the incision required is smaller than for bone plating; thus the trauma to the tissue is less.

4. Ambulatory treatment is possible thus reducing hospitalization.

INTERSCAPULOTHORACIC AMPUTATION FOR MALIGNANT TUMORS OF THE SHOULDER REGION

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Chicago, Illinois

THE treatment of malignant tumors about the shoulder is one of the most serious problems in surgery. The standard operative procedure for such neoplasms is the interscapulothoracic amputation, which consists in the removal *en bloc* of the forequarter, consisting of the upper extremity, clavicle, scapula, and all the muscles overlying the thoracic cage in this extensive area. The loss of limb itself is serious enough; but this amputation is so mutilating and severely shocking that the patient will not often submit to it, and the surgeon will frequently hesitate to perform it, even when the indications are definite.

Occasionally, such tumors are of a radiosensitive nature, such as the Ewing's sarcoma, and may be successfully treated without radical surgery. More often they are quite radioresistant, such as the osteogenic sarcoma or chondrosarcoma and will not respond to radiotherapy. All too frequently irradiation or local surgical excision of such lesions is attempted, only to be followed by local recurrence and sometimes by pulmonary or other distant metastases by the time interscapulothoracic amputation is considered. In addition, excessive irradiation of the shoulder region may lead sometimes to pulmonary fibrosis.

Recent observation of a case of chondrosarcoma which had been treated by local excision and irradiation with immediate recurrence, excruciating pain, and disability prompted the investigation of the entire subject of shoulder girdle amputation. The results of this study and case report are presented.

CASE REPORT

H. N., a 21 year old white male, presented himself for examination at the Tumor Clinic of the Michael Reese Hospital in January, 1938. He complained of excruciating pain, swelling, limited motion, and exquisite tenderness in the right shoulder region. He stated that he first noted a swelling in the right arm pit in May, 1937. This rapidly grew larger, became painful and tender until 1 month later it had reached the "size of a grapefruit," and the function of the shoulder joint had become markedly impaired. The roentgenogram (Fig. 1) shows the appearance of this lesion in June, 1937. At this time a local excision of the tumor was performed elsewhere. The histological diagnosis was fibrochondrosarcoma, grade 2. Intensive deep x-ray therapy and a superficial application of radium were administered after operation. Within 2 months a massive local recurrence had appeared and a second intensive cycle of x-ray therapy was given. A full course of injections of Coley's serum was administered intravenously. The lesion did not regress; the pain and disability of the extremity increased, and in November, 1937, the relatives of the patient were informed that the prognosis was hopeless and that nothing further could be done. The pain was agonizing so that morphine sulfate in one-fourth grain doses every 4 hours gave no relief. No active motions of the shoulder joint could be carried out; attempts at passive motion proved exquisitely painful. The skin overlying the shoulder and right side of the chest, anteriorly and posteriorly, was edematous and deeply pigmented from excessive radiation. The axilla was filled with a hard, immovable tumor about 12 inches in diameter.

The physical examination, other than that described, was essentially negative. The Wassermann and Kahn tests were negative, the red blood count was 4,460,000, white blood count 10,500, and hemoglobin 70 per cent. Roentgenograms of the chest showed no evidence of metastases. The roentgenogram of the shoulder January 18, 1938, showed an enlargement of the soft tissue axillary mass, increased periosteal proliferation in the metaphysis, and cortical and medullary atrophy of the entire shaft of the humerus (Fig. 2).

This neoplasm had proved radioresistant and the tissues were already so edematous from excessive radiation that continuation of this treatment was contra-indicated. The patient begged to have the painful limb removed. Because of the absence of pulmonary metastases, it appeared that the youth was entitled to interscapulothoracic amputation and he was referred to the orthopedic clinic for this procedure.

The forequarter amputation was performed on February 2, 1938, under ethylene and ether anesthesia according to the typical Berger technique. With the patient in the dorsal-recumbent position a 4 inch incision was made horizontally along the middle of the right clavicle and deepened to the periosteum. The sternoclavicular junction was then divided and the clavicle retracted forward and outward. The axillary and subclavian arteries were palpated, the subclavius muscle was incised, and the artery and vein were exposed (Fig. 3). This was the most difficult and time-consuming part of the operation and was accompanied by considerable bleeding. After exposure, first the subclavian artery and then the vein were each doubly ligated and divided between ligatures. The remainder of the procedure was practically bloodless. The 3 large trunks of the brachial plexus were then separately infiltrated with 2 per cent novocain and were divided. The lateral end of the incision was continued in racket-fashion to encircle the axilla. The pectoral major and minor muscles were cut across. The extremity was then rotated anteriorly and the

From the Michael Reese Hospital, Department of Orthopedic Surgery and the Tumor Clinic.

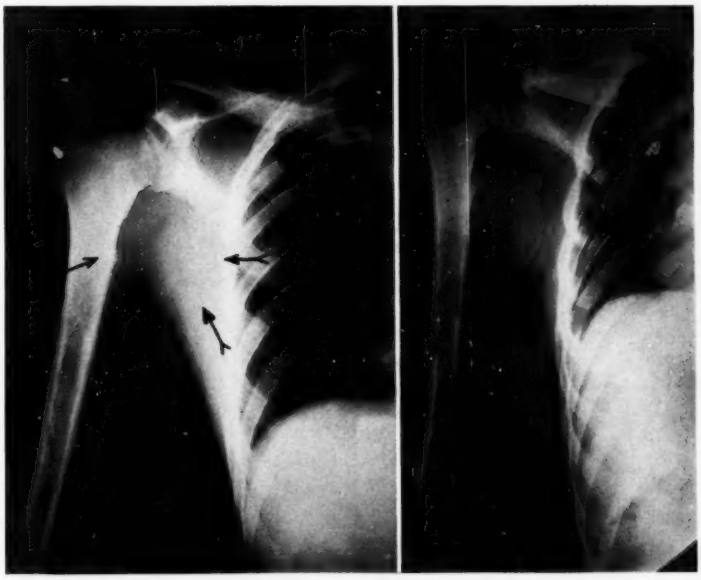

Fig. 1, left. Roentgenogram, June, 1937, of chondrosarcoma of right humerus. Note periosteal proliferation of the axillary border of upper metaphysis of the humerus and extensive soft tissue axillary tumor. (Courtesy Dr. Fred Shapiro.)

Fig. 2. Roentgenogram, January 18, 1938, showing enlargement of the axillary mass, increased periosteal proliferation and marked cortical and medullary decalcification of diaphysis of humerus.

posterior skin flap was raised. The trapezius muscle was divided, then the levator scapulæ and the rhomboid muscles. Finally, the serratus magnus and latissimus dorsi muscles were exposed and cut. The entire extremity remained attached only by the slender omohyoid muscle and some of the outer fibers of the trapezius which were divided, releasing the specimen, consisting of the entire forequarter. The remainder of the pectoral muscles and axillary content were removed. This left the entire thoracic wall devoid of its muscular coverings. A dependent cigarette drain was left *in situ* and the skin flaps were united by black waxed silk and silkworm gut sutures. Five per cent glucose in saline was administered intravenously throughout the operative procedure, a total of 2,000 cubic centimeters being absorbed. Because of a mild degree of shock (the blood-pressure dropping from 160/80 to 120/100 and the pulse accelerating from 80 to 110), 500 cubic centimeters of citrated blood were given as a transfusion after operation.

The postoperative course was uneventful. The day after the operation the patient was free of pain and profoundly grateful for the amputation. He was up and about on the seventh day and home on the fourteenth. The wound healed by primary intention. The patient at the time of writing is free of disease (Fig. 4).

Gross section showed that the tumor was confined to the humerus and closely surrounding soft tissues and had not invaded the musculature closest to the skin or to the thoracic cage (Fig. 5). The histological structure was that of a chondromyxosarcoma (Fig. 6). The axillary contents showed no evidence of tumor.

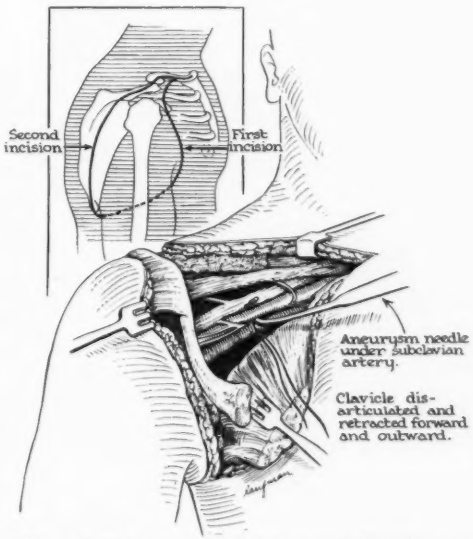
Second incision
First incision
Aneurysm needle under subclavian artery.
Clavicle dis-articulated and retracted forward and outward.

Fig. 3. Anterior approach for interscapulothoracic amputation; isolation of axillary and subclavian vessels. Insert shows racket incision.

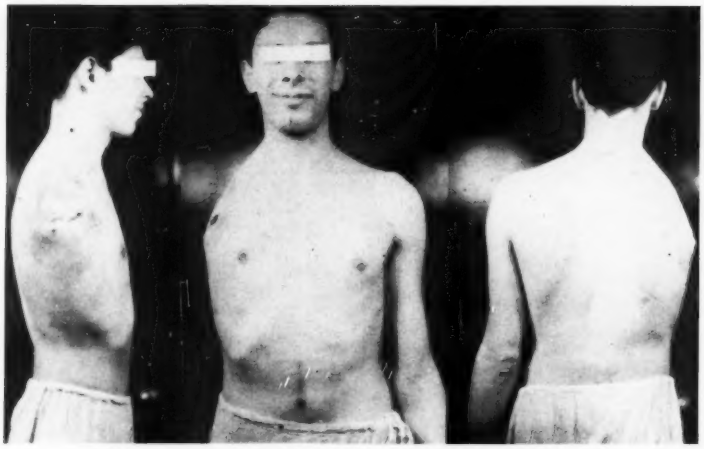

Fig. 4. H. N. Photographs 2 weeks after operation.

This mutilating operation is fortunately an infrequent one. According to Mueller, there were but 315 recorded cases up to 1907. The operation was first performed by Ralph Cummings in 1808 for a gunshot wound of the shoulder. The technique was independently perfected by Esmarch in Germany and Berger in France at about the same time (1887). The name of the latter has become attached to the operation and most textbooks of surgery now refer to it as the Berger amputation. Ollier, in 1884, was the first to recommend preliminary ligation of the subclavian artery as the first step in the operation following resection of the medial portion of the clavicle. This represented the greatest advance in the simplification of the operation for it becomes a practically bloodless procedure once the major blood supply has been controlled.

Radioresistant malignant neoplasms of the upper portion of the humerus, especially with extension into the shoulder joint or axilla, similar tumors involving the scapula or outer portion of the clavicle with axillary involvement, and primary radioresistant tumors confined to the axilla constitute the major indications for the performance of this operation. Most of the neoplasms necessitating this procedure have been histologically well differentiated sarcomas, as the fibrosarcoma, chondrosarcoma, or osteogenic sarcoma; other histological types have been described including the giant cell tumor (which, however, occasionally responds well to radiotherapy) and the neuroblastoma. The procedure is especially indicated if there have been multiple previous attempts at local excision of the tumor (as in the cases of Daland and of Leriche). In a number of cases this operation has been necessary for extensive traumatic lesions of the shoulder region, as in Cummings' original case. A few cases of intractable tuberculous or staphylococcic osteomyelitis about the shoulder joint that had not responded to less major surgical procedures have come to interscapulothoracic amputation. Mueller and Milch have written extensively on this particular indication.

First suggested by Franke, in 1913, for troublesome edema, axillary or retroclavicular metastases following radical mastectomy for cancer of the breast, the interscapulothoracic amputation for this purpose has been popularized within the past 10 years by the French school, particularly Prudente, Berard and Dargent. The latter have reviewed the literature on the subject exhaustively and maintain that the operation has been performed at least 16 times for fixed axillary recurrences following surgery for cancer of the breast. Of these 16, 25 per cent died at operation, 50 per cent developed later metastases, and only 1 case is known to have survived the procedure for as long as 4 years. Prudente, who performed this operation 5 times for such recurrences, specified particularly that it should not be undertaken in the presence of advanced ulcerating local recurrences, fixed chest wall or pleuropulmonary metastases, or fixed retroclavicular glands. Certainly, the operation should not be undertaken too lightly for this particular group of cases.

The immediate mortality following interscapulothoracic amputation has varied among numerous surgeons from the 5 per cent originally

Fig. 5. Gross specimen of chondrosarcoma of humerus.

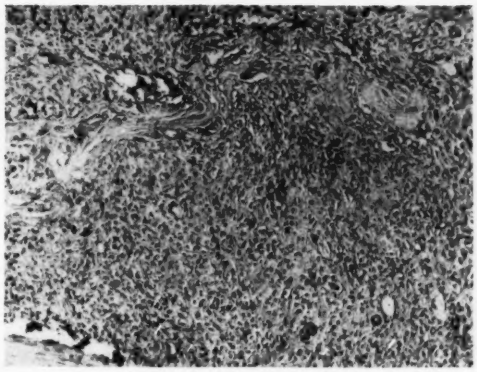

Fig. 6. Photomicrograph of chondromyxosarcoma of humerus.

claimed by Berger to 20 per cent recorded by others (18, 22). Preliminary subclavian vessel ligature, modern aseptic methods and control of operative shock, as by the injection of novocain into the cords of the brachial plexus preliminary to severing them, and the judicious use of stimulants and parenteral fluids during operation have done much to lessen the operative dangers of this amputation.

To justify the acceptance of such a mutilating procedure it must afford a reasonable expectation of prolonging life in addition to alleviating pain. Jembreau and Riche maintained there was an average life duration of at least 35 months following such amputation. Kawamura claimed 31.3 per cent of a large series of cases remained free of recurrence from several months to 16 years. Romankovic, on the other hand, observed recurrences in 66 per cent of his cases. In the American literature Jackson's case is outstanding. His patient was well for 13 years following interscapulothoracic amputation for chondrosarcoma before developing extensive local recurrence and intrathoracic metastases. There are, in addition, numerous individual cases remaining well from 1 to 5 years after this operation such as the cases of Leriche, Fischer, Daland, and Turco.

An analogous operation is sometimes performed for extensive disease, benign or malignant, of the proximal portion of the thigh where hip disarticulation will not completely eradicate the disease. This is known as the interilio-abdominal amputation. Occasionally, this operation becomes necessary for malignant bone tumors of the ilium or tumors of the soft parts of the outer surface of the pelvis extending into the hip joint and femur. Speed lists among the indications for this mutilating operation extensive dissecting aneurisms of the femoral artery and crushing injuries of the hip region with gas bacillus infections. The operation consists in the extraperitoneal removal of one half of the pelvic girdle with its attached lower extremity. According to Riswach this operation was first performed by Billroth in 1889, his patient dying several hours after operation. Jaboulay gave an exact description of the operative technique in 1894. Judin found in the literature 74 cases of this amputation reported prior to 1926. At least one-fourth of these cases are recorded in the Russian literature. As would be expected, the mortality associated with this operation is tremendously high, 44 of the above 74 cases failing to survive the operation.

A number of improvements in the technique of the interscapulothoracic amputation have been suggested. Most of the operators, like ourselves, have encountered considerable troublesome bleeding in the attempt to expose the subclavian vessels. This is often doubly difficult because of previous local operations or excessive radiation leading to a sclerotic fibrosis of the areolar tissues surrounding the major vessels. In addition, the vein lies anteriorly to the artery and is often inadvertently torn in the attempt to isolate the former.

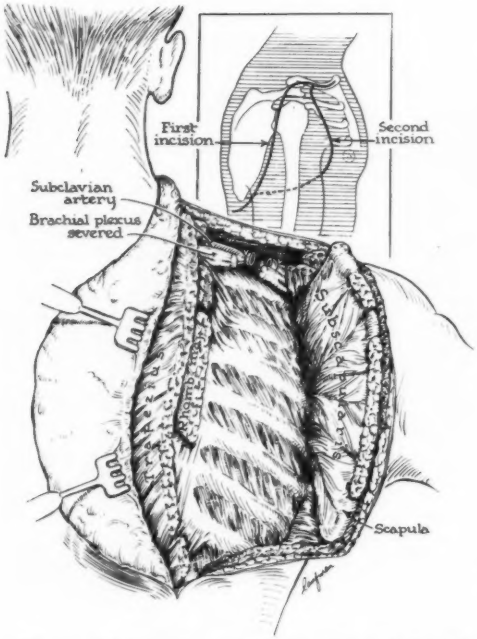

Fig. 7. Littlewood's technique—interscapulothoracic amputation. Posterior approach to subclavian vessels. Insert shows posterior and anterior lines of incision.

Patel maintains that preliminary division of the pectoral muscles and gently pushing back the shoulder girdle will make the subclavian artery and vein stand out more prominently. Littlewood has made a most important contribution to the simplification of this operation. He, too, described the difficulty in approaching the subclavian vessels through an anterior incision and usually required 2½ hours for the performance of the amputation. With his own modification, which will be described, he states that he has repeatedly accomplished the complete operation, including suturing of the skin flaps, in 25 minutes.

With the Littlewood technique (Fig. 7), the patient lies on the non-involved side. The first incision starts at the site of attachment of the sternal head of the sternocleidomastoid muscle, continues along the clavicle over the acromial prominence of the shoulder, then is directed posteriorly and downward along the axillary border of the scapula to below the angle of the scapula, and then continues mesially to about 2 inches from the vertebral column. The trapezius and the latissimus dorsi muscles are divided, then the levator anguli scapulæ, the rhomboids, serratus

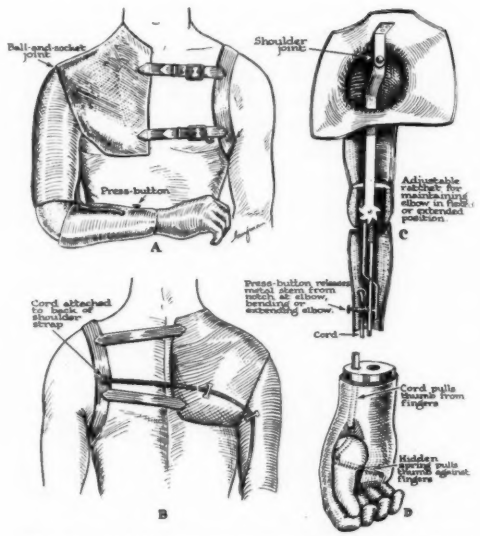

Fig. 8. Artificial upper extremity. Voluntary elevation of opposite shoulder motivates cord controlling finger motion.

magnus, and omohyoid muscles are separated from the scapula (Fig. 8). During this stage of the operation several small arteries are encountered, ligated and cut, principally branches of the suprascapular and posterior scapular arteries. Then the soft tissues are separated from the clavicle near the sternocleidomastoid muscle attachment and the clavicle is divided at this point with a Gigli saw. Then the subclavian muscle is cut. At this point the whole extremity falls forward away from the trunk and the subclavian vessels and the cords of the brachial plexus are fully on the stretch, standing out far more prominently than in the anterior approach and consequently more easily identified and ligated. Following the division of the cords of the brachial plexus and the ligation and division of the subclavian vessels, the skin incision is continued anteriorly in racket form as in the Berger operation, and the pectoral muscles are divided, delivering the specimen.

DeFrenelle has advocated the transscapular amputation as a substitution for the interscapulothoracic. This procedure is essentially like the Berger operation except that a large mesial portion of the scapula is left *in situ*. According to the author, the amount of exposed traumatized surface is diminished and the cosmetic configuration of the thoracic cage becomes less mutilated.

One would suppose, too, that there should be less likelihood of a scoliosis which is such a frequent sequel to the interscapulothoracic amputation.

A further useful modification of the classical Berger operation is that devised by Takhoff in 1922 and described by Linberg, in 1928, namely, the interscapulothoracic resection instead of amputation. In this operation, the pectoral girdle is removed with the upper involved portion of the humerus, the rest of the extremity remaining in place. The operation is feasible only if the vessel nerve bundle is not involved by tumor since the subclavian vessels may not be ligated.

In our case an artificial extremity, designed by one of us (D. H. L.), has been constructed, as shown in Figure 8. The fingers of the artificial hand can be moved by elevation of the opposite shoulder which exerts a pull on the cord. The elbow can be maintained in the flexed or extended position by the ratchet (Fig. 8, C) which can be released by the press-button as indicated.

SUMMARY

1. The authors have presented a case of chondrosarcoma of the upper portion of the humerus in which conservative treatment had proved futile. Following interscapulothoracic amputation there was striking relief of pain and at the time of writing the patient remains symptom-free.

2. The literature of this mutilating amputation has been reviewed, the technique described, and the indications for its performance discussed.

3. Several improvements in technique and alternative procedures have been mentioned. The modification of Littlewood seems particularly noteworthy.

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THE TREATMENT OF CHRONIC EMPYEMA BY CONTINUOUS HIGH VACUUM SUCTION

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IN the latest issue of a journal devoted to thoracic surgery, there were many articles describing various methods of the unroofing or thorocoplastic operations for the collapse of chronic empyema cavities. Because of the uniform and almost unanimous opinion that such a tremendous operation is essential to obtain results, I am pleased to submit an alternative method requiring little or no operative surgery together with a case report of a man slowly wasting away with empyema of 2½ years' standing to substantiate the theoretical and practical possibilities of this method.

There may be a tendency, because a disease occurs only infrequently, to treat it inadequately. Few, if any, procedures in thoracic surgery have become standardized to such a degree that further development would become unlikely or impossible. This in particular refers to the treatment of chronic empyema, a disease about which there is no question as to the objective the treatment should attain; but the means of obtaining this objective is a field which remains as yet within the scope of experimental surgery. Any procedure or device which, even in a minor way, contributes to the treatment of this discouraging condition is of distinct importance. The purpose of this paper is to record the theoretical and practical proof of a method of treating chronic empyema. A minimum of operative surgery is required and it is entirely possible that in some cases the patients would require no surgical procedure whatsoever.

Regardless of the method applied, the objective —the obliteration of the cavity—remains constant in the treatment of chronic empyema. We attempt to cause the walls of the cavity to approximate one another, to coalesce, to heal, and thus to obliterate the space. The cavity ceases to exist and is cured. The objective then is to move over one side of the wall to approximate the opposite wall and to keep it there until the two walls unite, or to interpose a second tissue into this space, such as muscle flaps or granulation tissue, thus obliterating the space with the aid of the new tissue. To effect this objective in the safest, surest, and easiest way possible is still a moot question.

When one considers the architectural pathology of a chronic empyema cavity and the tissues involved, it becomes increasingly obvious why this disease remains such a difficult condition to cure with any degree of certainty with even the most extensive and heroic operations. One would be apt, rather than call it a disease, to consider it a pathological syndrome, whereby the structures involved and the natural reactions of the tissues during repair are the very factors which spontaneously defeat the complete repair. To elucidate, it is only necessary to consider the pathological developments evolving in empyema.

In the formation of acute empyema the pus separates the two sheets of pleura, that on the inner chest wall and that on the outer surface of the lung. The lung is displaced inward to accommodate the pus and a layer of fibrin forms on the pleura in contact with the pus. If the pus is removed early, the breathing forces blow the elastic lung back into the concavity of the ribs. They unite and adhere and the condition is cured in the majority of cases if the pus has been overcome biologically and the evacuation has been accomplished efficiently.

If the pus is not removed or is only partially drained, the fibrin becomes organized, granulation tissue forms over the surface of the pleura; and the outer surface of the lung, which has been compressed, becomes progressively more fibrous. What had formerly been a thin flexible membrane, slowly but with increasing thickness becomes an unyielding, firm wall with no elasticity. The periphery of the lung, which formerly occupied the concavity of the ribs, becomes inflexible and shortened. If we assume that the inner curve of the ribs is a circle, then it is geometrically certain that a chord cutting that circle is necessarily shorter than the segment it cuts. In like manner the lung, moved inward by the pus and then solidified in this shortened condition, is no longer of sufficient length to fit where it belongs even if means were available to place it there.

If there are no methods of stretching this tough fibrous tissue wall and of holding it firmly against the outer wall until union is accomplished, we

Fig. 1. Roentgenogram of chest on admission.

Fig. 2. Roentgenogram 10 days after suction treatment.

overcome the dilemma by shortening the curved outer wall to such a degree that it would approximate the inner wall and have an opportunity to heal. This is the thorocoplasty or unroofing operation and is the most reliable means we have used to close the cavity of chronic empyema.

The facts mentioned are but the structural or mechanical causes which tend to prevent any simple means of cure. Of equal importance in delaying cure is the biological tendency of the tissues involved. The tissue which lines the walls of a chronic empyema cavity is perfectly analogous to the tissues of a surface wound elsewhere on the body. An open surface wound, uncovered by skin or mucous membrane has one predominating characteristic which is the crux of the situation in an empyema cavity the same as on a surface wound. When we speak of a surface wound as being healed, we mean that it has become covered with skin. Until it does become covered, it remains moist, weeping, infected, and constantly forms pus.

Skin extends out over the wound from the healthy edges in an attempt to place the wound surface cells where they belong, namely, beneath the surface. Sub-surface tissues have not the inherent properties of withstanding infections when they are accidentally placed in this strange surface environment. They continue to remain infected until skin covers it. The action of fibrous or scar tissue which forms and then contracts, assists in drawing the skin edges closer together. The time necessary for a surface wound to heal, therefore, is regulated not so much by the kind or degree of the infection, but by the time necessary to cover the wound with skin. It is a commonly known fact that a wound takes much less time to heal if the skin edges are pulled together even though the wound is yet infected, provided of course that gross drainage is controlled. The fact that the lining membrane of an empyema cavity is similar to an open, uncovered wound is the reason for the constant accumulation of pus. As long as the cavity exists, there will be a surface infection the drainage of which is within the cavity itself with the constant access to auto-infection. This process continues until the cells which form the lining membrane of the cavity are placed beneath the surface where they belong. This is accomplished by holding the two walls of the cavity together until they unite. What formerly was a surface membrane is now beneath the surface and healing ensues.

The outer wall of the cavity, because of its ribs, is the firmest part of the wall. From a structural viewpoint it would be more rational to allow this wall to remain as it is and move the inner wall, the side toward the lung, outward to the

Fig. 3. Roentgenogram 3 weeks after suction treatment. Sinus partly filled with lipiodol.

Fig. 4. Roentgenogram showing track 4 weeks after suction treatment.

other wall. This for obvious reasons has always been an impossibility. An approach in this direction has been attempted by insisting on blowing exercises by the patient. This procedure was of little practical importance except possibly in re-expanding the lung after drainage in acute empyema before adhesions have formed.

The atmospheric pressure acts equally on all surfaces, and with relation to an empyema cavity the pressure thrust is the same within the interior of the cavity as on all parts of the external wall of this cavity. If the pressure within the cavity is reduced, there is an unopposed pressure on the external surface of the walls toward the center of the cavity. The more the interior pressure is reduced, the greater will be the effect of the atmospheric pressure on the external walls of the cavity. Because of the resistance of the ribs which are better able to withstand the air pressure without displacement, the inner wall due to the air pressure thrusting on it through the respiratory passages would be displaced outward to the outer wall. If the weight of 50 miles or so of air could be directed with regulation on the medial wall of the cavity for a sufficiently long period, it was foreseen that the cavity walls would be squeezed together with eventual obliteration. The problem was to develop a means of reducing the air pressure within the cavity over a long period, allowing the atmospheric pressure to exert its weight on the external surfaces of the walls. Because the walls were re-enforced by ribs on the outside and were thick and leathery on the inside, it was recognized that nothing less than considerable physical force acting for an indeterminate period of time would be effective. The physical force referred to is that of the atmospheric pressure unopposed. To obtain the squeezing or compressing action of the most uniform, the most gentle, and yet one of the strongest of all forces, it is necessary to remove the air pressure from the interior of the cavity by suction. A further possible effect of suction applied to the interior of a cavity is that it will cause a congestion of the walls, and if enough suction is applied, it will produce oozing. This oozing would be conducive to formation of granulation tissue which would assist in filling up the space and enhance healing.

Several modes of using suction in the treatment of empyema, both acute and chronic, have been familiar for years. It was obvious that suction from the syphon-bottle system was useless because of the low degree of suction possible, and the constant attention necessary. Suction from water-faucet syphons is also impractical because of the tremendous amount of water necessarily

Fig. 5. Roentgenogram showing narrowing of track 6 weeks after suction.

Fig. 6. Roentgenogram showing shortening of track at 7 weeks.

wasted to obtain only a relatively low degree of suction. It was also impossible to think of using the standard tonsillectomy sucker because neither the patient nor the machine would tolerate such high speeds 24 hours a day, week after week.

An entirely new instrument was developed which corrected all the defects of other systems and fitted itself perfectly to this particular problem and an unforeseen number of other situations. The instrument consists of a vacuum storage tank whose vacuum is developed by an electric suction pump which automatically cuts in when the negative pressure is below 5 inches of mercury. The pump operates until the vacuum is built up to 17 inches of mercury and then the motor is automatically cut off until this vacuum has been utilized down to 5 inches again. An almost noiseless motor and pump can build up this vacuum in about 30 seconds to a minute, and for chest cases this amount will last for 5 to 6 hours depending on the type of application. When the instrument is used for other purposes such as duodenal suction, external duodenal fistula, or vesicovaginal fistula, the motor necessarily operates more frequently because there is a continuous flow of vacuum for evacuating purposes. The vacuum applied to the patient is controlled to any amount of pressure by means of a reducing valve, vacuum gauge, and bubble indicator. The control of this vacuum is absolutely exact and the instrument may be operated continuously for months without any further attention than plugging it into an electrical outlet and emptying the catch bottle. The instrument is designed primarily to deliver a high degree of vacuum, delicately controlled, and continued over a period of time which could possibly extend for a month or more. This instrument is light and compact and occupies a space of approximately that of a standard typewriter. There is an almost inaudible motor hum, lasting at the most a minute once every few hours so that there is no annoyance whatsoever to the patient. When the connection is plugged into the electric outlet, aside from regulating the flow with the reducing valve, there is no further attention necessary. Although the utility of this instrument in chest cases is particularly stressed in this paper, it is equally successful in other fields of surgery, such as gastric lavage, decompression of duodenum and intestine utilizing duodenal intubation, common duct drainage from a T-tube, and urinary bladder drainage following prostate and vesicovaginal surgery. It was found to be the instrument of choice in postoperative external gastric or duodenal fistulas.

Fig. 7. Roentgenogram showing track almost obliterated 8 weeks after treatment.

Fig. 8. Roentgenogram of chest after patient was discharged and cured.

The only difficulties found in the use of high continuous suction is that of correct size of rubber tube. Some tubes which will carry fluid are porous to air and will not hold a vacuum. A tube with too small a bore will soon plug due to a solid fragment clogging it or to the accumulation of deposit which is laid down within the tube. A tube with too large a lumen will allow air to pass through it without carrying along the fluid in the tube. One opening in the end of the tube, such as is used in the ordinary catheter, is much more liable to clog with fragments of débris. For best results it is necessary to make many auxiliary openings in the sides of the tube at the terminal 2 or 3 inches. It is also necessary in applying a suction tube into a chronic empyema cavity to have an almost air-tight fit at the entrance of the draining tract. This is obtained by enlarging the tract surgically and using a tube sufficiently stiff and of such a diameter that it is inserted into the tract with difficulty; and if there is leakage about the tube during the first few days, the contraction of the tissues soon forms a much closer fit.

While it is a modern tendency to express opinions only after the summation of a formidable array of statistical data, it is none the less true that one single isolated case beforehand may be the index of what a large series may prove at a later period. I mention this fact as an excuse for daring to publish a paper with but a single case in point. No bibliography is appended to this paper because no record could be found of chronic empyema having been treated by this method. It should be fully understood that suction drainage in empyema, acute or chronic, is well known and has been utilized for years, whereas no method has been discovered whereby a high vacuum amounting to 15 inches of mercury has been applied to the chronic empyema cavity for a period of 5 to 6 weeks. Previous uses of suction in chronic empyema have been solely for the removal of drainage, whereas this paper describes only the use of a high vacuum, not only for the removal of any collection within the cavity, but also for the collapsing of the thickened walls of the cavity by the high degree of suction obtained.[1]

CASE HISTORY

Mr. G. I., a white laborer, 52 years of age, was admitted to Rosebud Memorial Hospital on October 20, 1937, with a previous diagnosis of chronic empyema. There was no family history of tuberculosis nor any other illness of significance.

In July, 1935, the patient became ill suddenly with pain in his right chest on breathing. He developed a fever with

[1]Details regarding the vacu-aspirator may be obtained from the Perfection Manufacturing Company of Minneapolis.

chills and sweats. He is quite certain that he did not have a cough or pneumonia at the beginning of this illness, and what cough he did have came on subsequent to this illness. The pain was generalized over the right side of the chest and in the course of some weeks settled particularly in the right upper chest. A loose cough developed with night sweats, he began to raise sputum, and the pain in the side continued. He lost weight gradually and was confined to bed. He was certain that he had a high fever every day. After some weeks his chest was aspirated, and pus was obtained.

On August 3, 1935, a rib resection was done under local anesthesia. A drain was placed in the pleural cavity and considerable foul-smelling, thick pus and gas were obtained. He had made a satisfactory partial recovery when he was discharged September 28, 7 weeks following the rib resection, with a final diagnosis of empyema and bronchial fistula occasioned probably by a primary pneumothorax. Since that time, which is 2 years and 6 months since the original operation, he has been an invalid with a constantly draining sinus. The pus has always been foul and he has continually worn a dressing. There had been attempts made to cure his sinus by the injection of oil. If at times it became temporarily closed, he would develop chills and become acutely ill until the sinus would break and discharge.

He was admitted to the Rosebud Memorial Hospital on October 20, 1937, weighing 118 pounds while his average weight was 148 pounds. His general condition was very poor. His skin was gray and a foul discharge permeated the room. He gave the above history and stated there were about 1 to 2 ounces of pus on his dressings each day. Chief complaints were draining chest sinus, continuous loss of weight, weakness, chronic cough, and recurrent elevation of temperature.

The general examination revealed the following: Temperature 100.5 degrees, pulse 86. The tonsils were buried, pillars reddened, four lower incisors showed extensive pyorrhea. There were no neck abnormalities. Left chest appeared normal. Right chest contracted with all ribs showing. At level of tenth ribs at the posterior axillary line there were 3 openings which continuously discharged foul, thick pus. There were deep supraclavicular and infraclavicular depressions. Blood pressure, 118/72. The abdominal examination and examination of extremities revealed nothing. Red blood count was 3,700,000, and the white blood count 14,200 per cubic millimeter; hemoglobin was 58 per cent; urine was normal. Roentgenograms of the chest are illustrated in Figure 1. The Mantoux test and the test of sputum for tuberculosis were negative.

Lipiodol was injected into the sinus followed by roentgenogram to determine the length and direction of the sinus. It required too much lipiodol to fill the whole cavity although the length and direction of the sinus is well illustrated in Figure 2. It is impossible to determine accurately the cubic capacity of this type of cavity by the amount of fluid it will hold for the reason that when the fluid is injected up the track it is impossible to fill the track completely because the air cannot be thoroughly evacuated to allow a complete filling of the space. A diagnosis was made of chronic empyema with insufficient drainage. Under local anesthesia an incision was made 3 ribs above the opening of the sinus. Three inch sections of seventh, eighth, and ninth ribs were removed to allow exploration of the cavity. Considerable grumous material and pus were aspirated from the depths of the cavity and a probe could be entered into the cavity as high as the apex of the thoracic cage and inward to the upper part of the mediastinum. The cavity walls were thick and unyielding. A rubber tube with several side openings and about three-quarters of an inch in diameter was then forced into the opening and placed well into the cavity. The incision was then closed loosely over the tube. The operation was for the purpose of exploring the track and cavity and for the insertion of a tube of suitable size for high vacuum treatment.

Fig. 9. G. I. After 3 weeks high vacuum suction showing an early model of vacuo-aspirator.

When he was returned to his bed constant suction was applied to the cavity through the tube from the vacuaspirator.[1] Suction was begun at 2 inches of mercury and maintained 24 hours each day. An infant catheter had been inserted through the wall of the large tube and sealed with auto tire cement. This allowed irrigation of the cavity with Dakin's solution several times a day. With the negative pressure already in the cavity the irrigating fluid entered under the force of suction and very thoroughly washed out any further collections of pus and débris. Each day the degree of suction was increased and the cavity was irrigated. When the vacuum reached the degree of 10 inches of mercury and oozing of blood into the receiving bottle was noticeable, the suction was reduced in degree until the oozing ceased. In a few days it was found that suction could be increased to the previous degree without oozing of blood and such was done. There was some leaking of air between the tube and sinus wall for the first few days. Many substances were tried to stop this leakage but were to no avail, and later it was apparent that due to the suction and to the natural contraction of

[1]At the present time it is possible to obtain this type of drainage tube incorporating the irrigating channel from the American Cystoscope Makers.

the track, this air leakage ceased in a few days without further attention.

The patient was given a high caloric diet with forced feeding. His teeth were attended to and he was given iron and vitamin tonics. The tube from the vacu-aspirator was long enough to allow him complete freedom of his room and he soon learned to regulate the vacu-aspirator to any desired degree of suction and became highly interested in the treatment. He was allowed to disconnect the suction for sufficient periods during the day to eat his meals and for toilet facilities, after which he re-applied the suction himself. For the first 2 weeks when the suction was applied, he could feel the vacuum gripping the interior of his chest causing some little discomfort with some aching in his right arm but which did not require opiates. The tube was changed once a week more from curiosity than from necessity. Each subsequent x-ray picture showed a difference, not only at the site of the cavity but also in the remaining lung field, the clear area of which increased at each examination. After the first week there was very little drainage from the track which we attributed to the extreme efficiency of both drainage and irrigating systems which sterilized the cavity to a great extent. There was seldom more than a half to one dram of drainage in the bottle each day. After 4 weeks of continuous suction the cavity had been reduced to nothing more than a straight track which was fully occupied by the drainage tube as illustrated in Figure 2.

At this time the sinus consisted merely of a track only large enough to hold the catheter. The suction was continued and the catheter was withdrawn about an inch every few days. When the length of the track remained about 4 inches it was deemed sterile enough for spontaneous closure. The patient was discharged and returned 1 month later for examination. The sinus had stopped draining entirely and was completely healed. He had not had elevation in temperature for 2 months. His weight had increased since the beginning of the treatment. At the present writing, which is 7 months since he was discharged, the patient states that he is doing clerical work every day and has had no sign of discharge or his previous illness whatsoever. He is completely cured and extremely happy with the result.

CONCLUSION

A case is presented of a man incapacitated for 2 years and 6 months with chronic empyema whose weight and strength were decreasing constantly. The patient was completely cured by the use of continuous high vacuum suction applied to the interior of the cavity. A short description of the instrument perfected for this and all types of continuous suction is included with illustrations. It is recommended that this method be given a thorough trial before extensive and hazardous operations be resorted to for chronic empyema.

DIRECT INGUINAL HERNIA AND A METHOD OF FASCIAL REPAIR

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THE pathology of direct inguinal hernia is totally different from that of indirect or oblique inguinal hernia. A thorough understanding of the pathology is necessary if operation for repair of direct hernia is to be successful. That it has not invariably been understood and recognized is indicated by the relatively high recurrence rate in this type of hernia, as well as by the type of operation frequently seen performed or described. In the hands of competent surgeons the percentage of recurrence varies from 7 to 30 per cent and Andrews states that in about one-fourth of the cases operated upon for this type of hernia, the patient is made definitely worse by surgery.

PATHOLOGY

According to the usual textbook descriptions, the internal oblique muscle inserts into the lower borders of the 3 lower ribs, into the rectus sheath of which its aponeurosis forms 2 layers, and conjointly with the transversalis muscle into the pubic crest and pectineal line immediately behind the external inguinal ring. The conjoined tendon thus formed "serves to protect what otherwise would be a weak point in the abdominal wall (6)."

Recent investigations of the anatomy of the inguinal area lead the investigators (2) to believe that the conjoined tendon or aponeurotic falx as so described does not exist and that the structure so regarded and used by some surgeons in the repair of the inguinal floor is "merely an area in the anterior lamina of the rectus sheath rendered more prominent than the surrounding tissue through its insertion into bone."

In the type of individual prone to develop direct inguinal hernia there is often deficient development of the internal oblique muscle, particularly its lower border. Further, instead of its fibers becoming tendinous and inserting into the pubic crest and pectineal line its only insertion is into the rectus sheath at variable distances from the pubic crest.

This high insertion results in the formation of an inguinal triangle bounded by the rectus sheath, the lower border of the internal oblique muscle, and the inguinal ligament. This arrangement leaves a vulnerable spot in the inguinal floor which has for its support only the peritoneum and transversalis fascia. Anson and McVay, by measuring 95 unselected specimens, found that the length of the medial wall of the triangle, i.e., the distance from the insertion of the lower border of the internal oblique muscle to the pubic crest varied from 0 centimeters to 9 centimeters, 48 of the cases measuring between 2 centimeters and 5 centimeters.

We have found in practically all of our cases of direct hernias that the length of the medial wall ranges from 2 centimeters to 4 centimeters. It is obvious, therefore, that if repair is attempted by suture of the "conjoined tendon" to the inguinal ligament, approximation of the apex to the base of a triangle is being undertaken. The muscles forming the apex will very promptly raise it again, with resultant weakening of the inguinal floor and probable recurrence of the hernia.

In addition to the pathology already present, the external inguinal ring is, in our experience, nearly always enlarged, so that operative procedure relying largely on the aponeurosis of the external oblique muscle for reconstruction of the inguinal floor will find this structure inadequate at the most important point, namely, the lower portion of the inguinal area. It is here that most recurrent hernias are found.

Harris and White, in an interesting investigation of the length of the inguinal ligament in direct and indirect hernia, measured this ligament in 500 patients. They found that individuals with an inguinal ligament of less than 11 centimeters had slight tendency toward the formation of inguinal hernia of either type and that hernias occurring in individuals whose inguinal ligament measured from 11 to 15 centimeters were of the indirect type, while in those whose ligaments were from 15 to 19 centimeters the hernias were of the direct type. They found, further, that the longer the inguinal ligament, the deeper the pelvis; and conversely, the shorter the ligament, the shallower the pelvis. Their conclusions in regard to the formation of direct hernias were that in cases in which the inguinal ligament was long, there was relative shortening of the distance between the anterior-superior iliac spines with greater inclination of the pelvic floor, thus causing intra-abdominal pressure to be exerted mainly near the midline, producing the direct type of hernia.

From the Surgical Service, U. S. Marine Hospital.

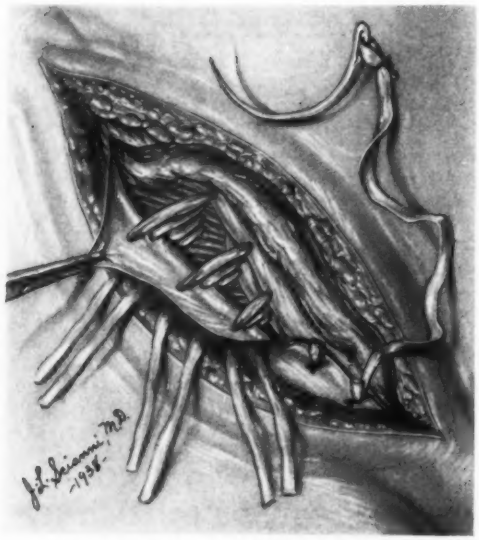

Fig. 1. The sac has been disposed of, the transversalis fascia has been closed, and reconstruction of the inguinal wall has begun.

Fig. 2. Reconstruction of the inguinal wall has been completed by the overlapping of the aponeurosis.

ETIOLOGY

Direct hernia is always acquired, that is, so far as the hernia itself is concerned. The anatomical defect is already present and intra-abdominal pressure gradually produces a bulging through a weak spot in the abdominal wall. It is our opinion that this is a gradual process and that the sudden production of a direct hernia rarely occurs. Its possible extension through the external ring with corresponding spreading of the anatomical structures of the inguinal triangle due to sudden increase in intra-abdominal pressure may produce pain and bulging, leading to the belief that the hernia is traumatic in origin.

Practically speaking, direct hernia occurs only in the adult male. Less than 1 per cent occur in women. Seward Erdman concludes that the enlarged external abdominal ring is an important factor in the causation of direct hernia in the male.

TECHNIQUE OF REPAIR

Cure of direct inguinal hernia is obtained only if the inguinal triangle is closed completely and permanently. Important factors in effecting such a closure are the selection of such structures for the reconstruction of the inguinal floor as can be approximated without tension, the employment of fascia-to-fascia suture as far as possible and the use of fascia lata, as described by Gallie (4, 5).

The obtaining of fascia lata strips is a simple procedure and is done by an assistant during the course of the operation. A longitudinal incision about 3 inches long is made over the lateral aspect of the thigh approximately at the level of the perineum. Incisions in the same direction are made in the fascia lata about 1 centimeter apart. Across the upper ends of these incisions a transverse incision is made, thus freeing the upper portion of the fascial strips. The Bartlett[1] fascia stripper is then used to free the strips subcutaneously, at the same time cutting them off distally after the desired length has been freed. The thigh incision is closed with a few skin sutures or clips. For convenience of the operator and assistant, the thigh opposite the side on which hernia repair is being done is used. One end of a fascial strip is threaded through a Gallie needle for a distance of about 1.5 centimeters and secured by a suture of fine silk. Care is taken to avoid bulk at this point; if necessary, the threaded end of the strip is trimmed with scissors. The prepared strips are then placed in a small covered tray between layers of gauze moistened with saline until needed by the operator, who in the meantime has proceeded with the operation at the site of the hernia.

Incision for the hernioplasty is made so as to expose the pubic spine below and extend some-

[1]Recently devised by Willard Bartlett, Sr., St. Louis, Missouri.

what cephalad to the internal ring above. The aponeurosis is exposed and incised into the external ring, the incision being nearer the lateral than the medial pillar of the ring. The cord is pulled up, isolated, examined for a possible indirect sac, and retracted lateralward.

The sac is located and the condition of the transversalis fascia is noted. If this structure forms a definite continuous layer over the sac it is incised. The sac is picked up and the preperitoneal fat is carefully dissected away, particular caution being observed to avoid damage to the bladder which often lies on the medial wall of the sac. The peritoneum of the sac is opened and the redundant portion is cut away. As the direct sac usually has a broad base, closure is best achieved by a continuous or purse-string suture. For the same reason, in some instances the sac may be treated by inversion with a purse-string suture without being opened.

As a preliminary step in the reconstruction of the inguinal floor or wall, closure of the transversalis fascia, which frequently is well developed and of considerable strength, provides an additional layer and strengthens the new wall to that extent. Closure may be effected by suture of the rent frequently found in this layer, or of the incision made in dissection of the sac with fine chromic catgut; or, if bulging, the redundancy may be disposed of by a purse-string suture. Sometimes the upper portion is strong and well developed, the lower portion thinned out and weak; in such cases the upper and stronger portion is brought down without tension and included in the suture to be described. It seems reasonable to assume that smooth closure of the transversalis fascia in addition to providing an extra layer of some strength serves to distribute the stress of intra-abdominal pressure evenly against the outer layers of the wall under construction.

To obtain the next layer for the reconstruction a curved incision is made along that portion of the anterior rectus sheath posterior to the aponeurosis of the external oblique. This incision is made near the lateral margin of the rectus sheath and extends cephalad from the pubic crest for 4 or 5 centimeters, curving slightly outward. Adequate exposure of the sheath, consisting at this level of two of its three layers, is obtained by medial and forward retraction of the aponeurosis, its third layer. The portion of the sheath lateral to the incision is drawn lateralward by traction on its cut edge and sharp dissection from the underlying rectus and pyramidalis muscles. This procedure furnishes a fascial flap which can be approximated without tension to the lower portion of the inguinal ligament thus covering a most vulnerable area. Due to enlarged external rings present in most cases, overlapping of the aponeurosis of the external oblique does not always provide a strong, firm closure, hence the addition of the rectus sheath flap to the constituents of reconstruction. The anterior sheath appears to be adequately replaced by the medial leaf of the aponeurosis, the edge of which is to be sutured to the shelving edge of the inguinal ligament.

The component parts for the reconstruction of the inguinal floor having been exposed, suture is begun, with strips of fascia lata as suture material. Interrupted sutures are inserted as shown in Figure 1. Starting at the lower end of the inguinal ligament the first suture or fascial strip is passed from without, i.e., lateral and inferior to the ligament under its shelving edge. It is next passed through the rectus sheath flap near its free margin and also through the transversalis fascia if this structure is available and not previously closed by an alternate method. The direction of the needle being reversed, it is passed through the shelving edge in a direction away from the femoral vessels, then back through the medial leaf of the incised aponeurosis near its free margin, thence through the lateral leaf just above the shelving edge of the inguinal ligament. In insertion of the first suture a portion of the periosteum of the pubic spine is included. The end of the strip is clamped, the needle is left on, and the exposed strip and needle are protected by gauze. Other fascial strips, slightly more than a centimeter apart, are inserted in this manner to the internal ring. In the upper part of the inguinal floor, the lower borders of the internal oblique and transversalis muscles are used instead of the rectus sheath, as these muscles can be approximated to the shelving edge of the inguinal ligament in this location without tension.

After insertion of all the fascial sutures, starting with the lowest, traction is made on both ends, and a silk suture is passed through the ends at the level of the aponeurosis and tied twice so as to include the entire width of both strips. The short end is cut off slightly more than a centimeter from the silk suture; the long end carrying the needle is left for further use. The other strips are secured similarly, both ends being cut off, however. Traction on the lower or originating end of the fascial strip approximates the innermost layer of the closure, whereas traction on the upper or emerging end of the strip brings over to the inguinal ligament the medial leaf of the aponeurosis, so that accurate apposition of the inner layers can be obtained and inspected before these layers are cov-

ered by the medial leaf of the aponeurosis. The lateral leaf of the aponeurosis is then overlapped (Fig. 2), being sutured to the surface of the medial leaf with the fascial strip first inserted, the needle having been left on for this purpose. The aponeurosis is closed above the internal ring by one or two interrupted sutures if necessary. The subcutaneous fascia and fat are closed carefully over the cord which lies outside the aponeurosis, and the skin is closed after careful hemostasis.

This method of closure reconstructs the inguinal floor in its lower part, the vulnerable point for recurrence, with 4 fascial layers, the transversalis fascia, the rectus sheath, and the 2 overlapped flaps of the aponeurosis. Closure is further reinforced by the use of fascia lata in approximating and overlapping these structures.

Needless to say, meticulous technique as regards asepsis is necessary, as infection may result in loss of the reinforcing fascial strips. In our experience of over 100 cases repaired by this method infection has not occurred. To date no recurrence has been noted, but the method has not been in use sufficiently long to make a definite statement as to recurrence. It is felt, however, that a method employing structures that are for the most part fascial in origin, and that can be approximated without tension will result in a minimum of recurrences. It is our opinion that the use of fascia lata definitely reinforces the closure, and is, therefore, an important factor in the prevention of recurrence.

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EDITORIALS

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ATROPHY OF BONE

EVERYONE familiar with the treatment of injuries of bone, particularly fractures, knows that prolonged fixation with plaster of Paris inevitably leads to atrophy of bone. What brings this about may not be well understood. It is known that stasis of blood in an extremity, voluntary disuse of an extremity, and various types of inflammatory lesions of joints which produce a painful fixation spasm will lead to atrophy of bone. Vascular conditions which cause pain will lead to atrophy of disuse because of the painful condition, although ischemia in itself does not produce atrophy of bone but rather causes a sclerotic change in the bone.

Another type of atrophy of bone which is rather well recognized by those interested in orthopedic surgery is that known as Sudeck's atrophy. A rather definite understanding of this condition has evolved through the efforts of several workers, but much remains to be learned about this condition. Certainly it seems in many cases to be a part of a general symptom complex predominated by some type of vascular neurosis as yet not completely understood.

Between the atrophy of disuse and Sudeck's atrophy lies a group of conditions which are commonly known as post-traumatic painful atrophy and, as a rule, involve bones adjacent to joints and also involve the joints themselves. Some may claim that these conditions are in truth Sudeck's atrophy. Yet one does not see the extreme degree of vascular change usually associated with the more acute forms, usually known as Sudeck's atrophy. Others may feel that these forms of so called post-traumatic painful atrophy are only forms of the atrophy of disuse, but they often may appear in spite of an amount of use usually sufficient to prevent the occurrence of atrophy.

One could mention many other types of osteoporosis, such as senile osteoporosis, which seems to be seen more often than in previous years. All of these conditions stress the importance of more complete knowledge of the physiology of bone and its pathological reactions to the various changes to which it may be subjected, such as the following trauma, disuse, and disease.

As our knowledge improves, it is safe to predict a more comprehensive approach to the treatment of many conditions. Besides a more complete knowledge of the physiology of bone, a better understanding of the physiology of the circulation of the extremities must be had before these conditions can be understood. Finally, as our knowledge of the chemical composition of the human bone and tissues and of the physiologicochemical reaction of bone is improved, much light will be thrown on this interesting subject. RALPH K. GHORMLEY.

THE RÔLE OF SURGERY IN THE RECOVERY OF THE TUBERCULOUS INDIVIDUAL

TUBERCULOSIS once considered a contra-indication to surgical intervention now responds most favorably to this method of treatment. Not many years ago the presence of tuberculosis, particularly pulmonary disease, frequently deterred surgeons from undertaking necessary surgical operations, while more recently many tuberculous individuals have sustained harm from the over-zealous activities of an awakened surgical profession. Between these two extremes lies a middle course which offers to the patient maximum possible benefit, yet at the same time protects him from ill advised operative trauma. A better understanding of the problems involved in the treatment of this disease by surgeons and medical men alike will lead to more satisfactory results and a lower operative mortality rate.

Tuberculosis is a constitutional disease which manifests itself clinically by its localizations in various tissues and organs of the body. From the site of original implantation the organisms may become distributed widely throughout the body to form secondary foci from which later develop the symptom producing lesions recognized as clinical tuberculosis. Although commonly single, multiple areas of disease occur with sufficient frequency to render routine search for them mandatory. A complete and thorough study of the patient from head to foot must be made in order to discover all tuberculous and non-tuberculous disease, for it is only through such intensive study that the patient's best interests can be served and a balanced judgment as to proper treatment rendered. Therapy must be directed to the patient as a whole and not merely to a local lesion for complete results.

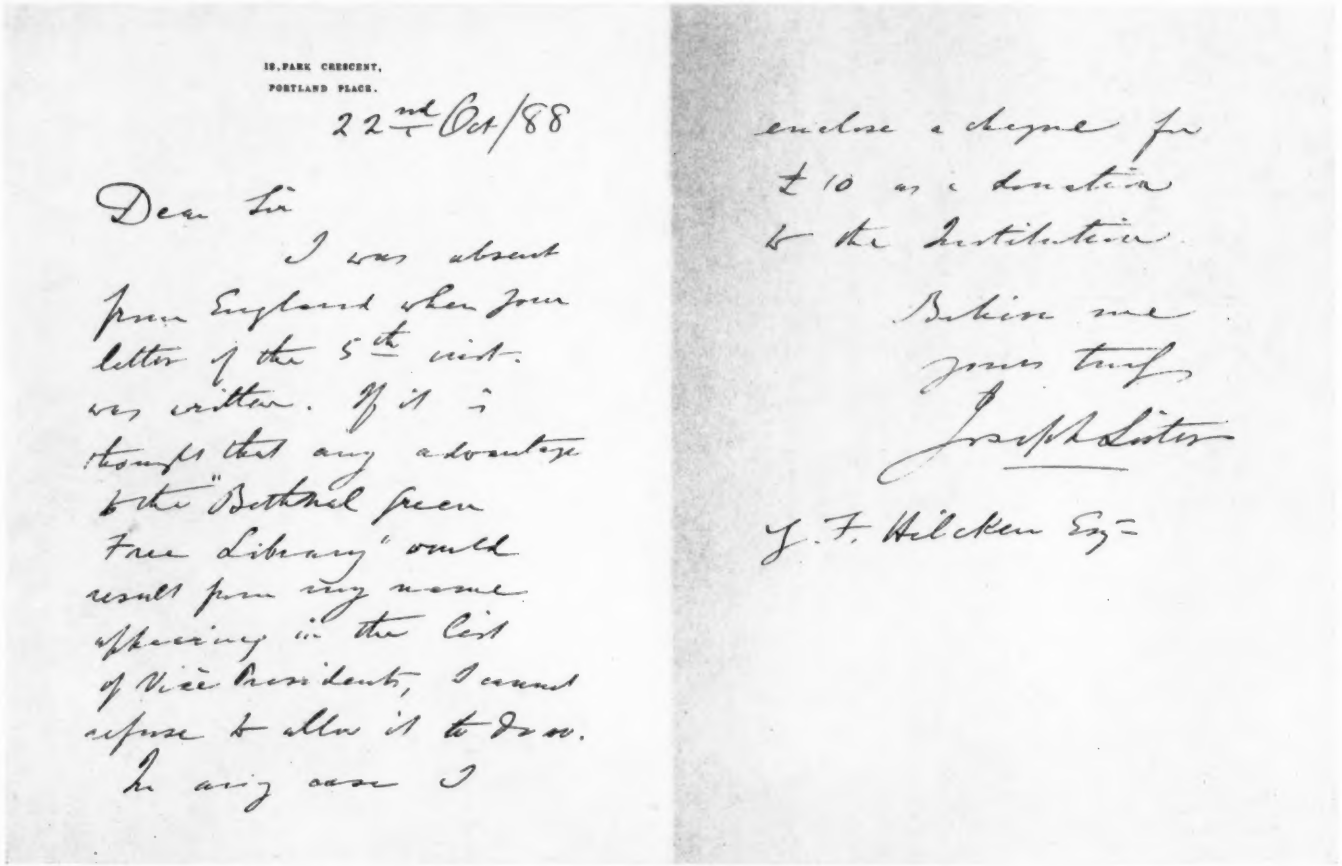
No field of medical endeavor offers more favorable opportunity for group work than does the adequate handling of tuberculosis in all its protean manifestations. The phthisiologist, internist, surgeon, roentgenologist, cardiologist, urologist, otolaryngologist, bronchoscopist, oculist, proctologist, pathologist, and various other specialists may at some time or other be called upon to contribute their share toward rehabilitating the individual. It is eminently desirable that the phthisiologist and internist be surgically minded and appreciate the possibilities of surgical treatment and its modern developments; but it is equally as important that the surgeon either understand tuberculosis, its response to treatment, and the dangers of its dissemination or permit himself to be guided by those who do. It is as unwise for the medical man unskilled in surgical therapy to attempt such work, as it is for the surgeon unversed in phthisiology to undertake this type of surgery alone. Each has his own sphere, with close co-operation the keynote to success.

Fundamentally surgery does not cure tuberculosis as it may cure other types of disease; for in tuberculosis, because of the very nature of the process, no single operation or series of operations can completely rid the patient of all foci of the infection. In spite of such limitations it may be and frequently is the deciding factor in bringing about recovery, yet, unless the patient possesses or develops that indefinable something known as resistance against tuberculosis he will not conquer the disease even with the best surgical attention. Under suitable circumstances the surgeon may be able to resect an apparently local focus of the disease (nephrectomy, salpingectomy, lobectomy), but even at best he is unable to remove all the process from the local system to say nothing of the whole body. Drainage operations for tuberculous abscess

(psoas, perinephritic or pleural) may relieve local symptoms but never eliminate all local disease. So much the more do the indirect procedures (spine fusion, thoracoplasty) which do not touch the local lesion but merely alter local function by immobilization or immobilization and compression, fail to relieve the patient of all his tuberculosis although they may aid very materially in inducing recovery. The effect of the surgery is mechanical, altering physiological conditions and correcting physical handicaps to permit the patient to combat the infection under more favorable circumstances. All manipulations should be carried out with the minimal trauma, both surgical and anesthetic, compatible with the operation required. Speed of operation may be of much less importance to the patient than gentleness in handling tissue. If anyone must be handicapped let it be the surgeon rather than the patient. Excessive trauma, hemorrhage, shock, or anything which lowers the patient's resistance may be followed by a flare-up or dissemination of tuberculosis. Blood transfusion may replace blood loss, but it does not compensate for other damage which has been done, and this damage may be considerable.

Tuberculosis is a serious disease, carrying with it a high morbidity and mortality rate. No patient suffering from it has any chances to throw away. Advantage should be taken of any and every method which may contribute even in small measure to the patient's ultimate recovery. A 3 months' "cure" of this disease does not exist. Half way measures may delude the patient as well as the physician for a time but rarely gives permanent results. An adequate treatment for tuberculosis should be an intensive composite program in which surgery plays a minor or major part, but never the complete rôle. Individual circumstances and the well balanced clinical judgment must determine when, where, and how surgery shall be utilized, but adequate constitutional treatment must always be combined with it if best results are to be obtained.

THOMAS J. KINSELLA.



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THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

THE appearance of *Cancer; Its Diagnosis and Treatment*,[1] by Cutler and Buschke, marks a new trend in cancer therapy. Medical historians will be able to trace the development of knowledge concerning cancer by the men who wrote the books about it. The foundations of our modern knowledge of the treatment of cancer were laid by outstanding surgeons of the past century such as Warren, Gross, Paget, and Butlin. All of these men took a special interest in cancer and wrote good books about it. The pathologists next dominated the trend of thought about the disease. Borst, Ribbert, Ewing, Masson, and Menetrier classified and described its multitude of forms in books of permanent worth. Today radiation has taken an important place in the treatment of cancer and we find the radiotherapists writing books about it.

That by Cutler and Buschke is the first book of its kind to appear in this country. Both of the authors are equipped with a broad knowledge of radiotherapy. They have had the assistance of a third well trained radiotherapist, Simeon T. Cantril. They have written a book of 757 pages which aims to present the essential clinical features and the preferred methods of treatment for the more common forms of cancer. The first chapter deals admirably with the biological effects of radiation and the general principles of its clinical application in cancer. Two short chapters on biopsy and on the spread of cancer follow. Each of the 39 remaining chapters deals with a regional type of cancer. A well chosen bibliography of the more recent papers concerning each form of cancer is appended at the end of the book and a name and subject index completes it.

Many of the 346 illustrations included are good reproductions of roentgenograms while others are well chosen clinical photographs and drawings. The book is printed in clear type on glossy paper.

This book offers a great deal of information concerning the principles and technique of radiotherapy as it has been practiced by Coutard and his associates at the Radium Institute in Paris. The chapters dealing with tumors in the head and neck in particular are the best that have been written in English. The chapters on cancer of the uterus, too, are admirably done. The authors are at home in discussing these forms of cancer, for their treatment has in general been turned over to radiotherapy. The pathology of these lesions is comparatively simple and stereotyped, and surgery does not often come into consideration.

This cannot be said for other forms of cancer, and in dealing with them Cutler and his associates are often inadequate. They lack that thorough familiarity with modern pathology that is necessary to anyone who attempts to classify malignant neoplasms. This is illustrated by the manner in which they deal with soft part sarcomas. They have lumped all forms together under the title of "neurogenic sarcoma," and infer that Ewing believes that most fibrosarcomas, liposarcomas, and myosarcomas are of "neurogenic" origin. The authors also display in many places in their book a lack of understanding of the fundamental principles underlying the surgical treatment of cancer as well as of modern surgical technique. These failings are most evident in their discussion of cancer of the breast in which they have included a description of operative technique. Elsewhere they have wisely avoided descriptions of surgical technique.

To sum up, this is a book which is a valuable contribution from the radiotherapeutic point of view, but which does not deal adequately with the surgery of cancer. It is well to keep in mind, in these times when radiotherapy is being recognized somewhat belatedly as an exceedingly important part of the treatment of cancer, that surgery is still by far the most important weapon against the disease.

C. D. HAAGENSEN.

THIS newest addition to the textbooks on otolaryngology, *Diseases of the Ear, Nose and Throat*,[1] deviates somewhat from the usual presentation employed by most authors and follows the established custom only in a general way. Dr. Lederer's background and association with clinicians has enabled him to correlate the subject matter and present it in a readable and entertaining full-length volume of 800 pages. He has made an effort to meet the needs of general practitioners and students and also to serve teachers and specialists.

The anatomical illustrations are numerous and very well done, particularly those relating to the paranasal sinuses. A welcome addition is the chapter on diseases of the mouth and one on swellings of the neck, both subjects being well presented and accompanied by good photographs. In the chapter on correlated considerations the author calls attention to the general aspect of diseases as they relate to the ear, nose, and throat. Among others, these considerations include a differential diagnosis of headache and the causative factors of cough.

[1] CANCER; ITS DIAGNOSIS AND TREATMENT. By Max Cutler, M.D., and Franz Buschke, M.D. Assisted by Simeon T. Cantril, M.D. Philadelphia and London: W. B. Saunders Co., 1938.

[1] DISEASES OF THE EAR, NOSE AND THROAT. By Francis L. Lederer, B.Sc., M.D., F.A.C.S. Philadelphia: F. A. Davis Co., 1938.

Surgical treatment is generally given in a short concise outline style useful perhaps more to the student than the practitioner. The text is on excellent paper with clear, readable type. No doubt this book will find a broad use among students and practitioners alike. JOHN F. DELPH.

THE simple aim of *Anatomie Chirurgicale du Crâne et de l'Encéphale*[1] is to present the facts of cranial anatomy in such a way as to make them readily available for their practical employment by the neurological surgeon. The authors, a surgeon and an anatomist, have succeeded in their purpose. The work is entirely new, and while little of actually new anatomical material could be expected, the general plan of the book is such that it sustains interest and makes for easy reading.

Following a plan of convenient arrangement, the general anatomy of both the bony cranium and the enclosed brain is reviewed, together with special descriptions of such regions as the sellar and suprasellar areas, the ventricles, the posterior fossa, and the upper cervical-foramen magnum area. In all this, the presentation is not noteworthy for any especially original treatment; in fact, it is rather traditional, with enough clinical pathology woven into the descriptions, however, to freshen the topic somewhat, but it seems that the authors do not forget for a moment that their readers will be clinicians with an interest in the practical application of anatomy. The illustrations are for the most part simple drawings, effective and useful but never elaborate. They are practically all originals. While the book is hardly an atlas because of the preponderance of text material, and though the illustrations are not as life-like or artistic as some found in other modern texts of anatomy, yet the illustrations serve their purpose fully because they are placed as closely as possible to their descriptive text, and thumbing through pages to a referred figure is never necessary. The treatment of the dural venous sinuses is excellent, and some of the photographs of intracranial arteriographs are especially good.

This is, indeed, a book worth reading and owning. Its greatest delight lies in the directness and simplicity with which it is written. There is no padding, no repetition. It is well balanced and logically arranged. The written text is free of style except for a characteristic manner of constantly but proportionately referring to the pathological state.

JOHN MARTIN.

[1] ANATOMIE CHIRURGICALE DU CRÂNE ET DE L'ENCÉPHALE. Published under the direction of André Latarjet. By Charles Clavel and Michel Latarjet. Paris: G. Doin & Cie, 1938.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

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